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OF MEDICAL PRACTICE

INCLUDING

MEDICINE SURGERY OBSTETRICS GYNAECOLOGY AND OTHER SPECIAL SUBJECTS

Under the General Editorship of

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VOLUME FIVE

ENDOSCOPY OF RESPIRATORY TRACT *TO* GOITRE

LONDON

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BELL YARD, TEMPLE BAR

1937

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ENDOSCOPY OF THE UPPER RESPIRATORY AND ALIMENTARY TRACTS

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Reference may also be made to the following titles:

1.—DEFINITION

407.] Peroral endoscopy is a convenient term used to cover the examination of the interior of the larynx, trachea and bronchi, oesophagus, and stomach by direct laryngoscopy, bronchoscopy, oesophagoscopy, and gastroscopy. The examination is effected by the use of rigid tubes of various shapes and lengths passed through the mouth under direct vision to the part to be inspected.

Historical   This method was first devised by Kirstein in 1894 for the larynx, and Killian probably first realized the possibility of straightening out the bronchus with a rigid tube; he was the first to remove a foreign body from the bronchus (1897). The history of oesophagoscopy goes much further back than that of bronchoscopy and is chiefly associated with the names of Stoerck and von Mikulicz.

The chief difficulty encountered in early days was the illumination of the field of vision. Originally this was provided by a head-lamp worn on the forehead, the beam of light being reflected down the tube. This was difficult to centre in a narrow tube and Brünings's invention of an electroscope with a handle to which the tubes could be attached was a great advance, the light being reflected down the tube in parallel rays from a small slotted mirror through which the observer could look. This proximal lighting is not always satisfactory in long tubes and Chevalier Jackson suggested the use of a distal light. A tunnel in the wall of the tube contains the light-carrier, and the small electric bulb which emerges into the lumen near the distal end lies in a recess in the wall of the tube. This method of distal illumination is now largely used, but is not without drawbacks, as the small lamp is apt to be soiled by blood or secretions which may obscure the field of vision.

Instruments   Peroral endoscopy cannot be satisfactorily performed without a carefully selected set of instruments to meet all requirements. No single instrument will suffice, and, in order to examine patients of all ages and sizes, various sizes of laryngoscopes, bronchoscopes, oesophagoscopes, and gastroscopes must be at hand.

2.—ANATOMY OF THE PHARYNX, LARYNX, TRACHEA, AND BRONCHI

Pharynx   The pharynx extends from the base of the skull above to the level of the sixth cervical vertebra below, where it becomes the oesophagus. It is usually divided into three parts: the nasopharynx, the oropharynx, and the laryngopharynx. It is chiefly with the latter portion that direct examination is concerned. This part, the pars laryngea, or hypopharynx, lies behind the larynx and is normally closed, as the posterior wall of the larynx (crico-arytenoid region) is closely applied to the vertebral column. The upper part of the pharyngeal aspect of the larynx is

situated behind and below the base of the tongue and consists of the epiglottis and aryepiglottic folds which bound the superior aperture of the larynx. Lower down is the pyriform fossa on either side, a depression between the aryepiglottic folds and the inner aspect of the thyroid ala.

The larynx extends from the aryepiglottic folds to the lower border of *Larynx* the cricoid cartilage and is usually divided into three parts: the vestibule, the glottis, and the subglottic space. The vestibule is cone-shaped and is bounded in front by the laryngeal surface of the epiglottis, laterally by the aryepiglottic folds as they slope down towards the edge of the false vocal cords, and posteriorly by the front of the arytenoid cartilages and the interarytenoid region. The glottis is the chink between the vocal cords; the true vocal cords bound the anterior two-thirds, and the vocal processes with the mesial surface of the arytenoids bound the posterior third. The subglottic space lies below the true vocal cords. Here it is rather narrow, but it broadens out below towards the trachea. The *Trachea* trachea begins at the lower border of the cricoid, which lies opposite to the lower border of the sixth cervical vertebra, and ends by dividing into the two main bronchi at the level of the fifth dorsal vertebra. Before *Bronchi* dividing it passes somewhat to the right, so that the right main bronchus, which is slightly the larger, seems to be the continuation of the trachea. For this reason foreign bodies are much more likely to fall into the right bronchus than into the left, and the bronchoscope also passes into it more easily. The right main bronchus gives off an eparterial bronchus which passes above the pulmonary artery and serves the upper lobe of the lung. As it makes rather a sharp angle with the main bronchus it is difficult to examine with the bronchoscope (see Fig. 2).

The main bronchi divide into inferior branches and the spur between these can be well seen. The whole bronchial tree can be mapped out by radiography after the injection of iodized oil (lipiodol).

In the adult male the average measurements are:

From upper teeth to trachea   –   –   –   15 cm.
From upper teeth to bifurcation   –   –   27 cm.
From upper teeth to right upper-lobe bronchus   29·5 cm.
From upper teeth to secondary bronchi on left
    side   –   –   –   –   –   32 cm.
Diameters of trachea –   –   –   –   14 and 20 mm.

3.–PREPARATION OF PATIENT

A careful history of all patients about to undergo direct examination *General* of the air- and food-passages is naturally taken. An X-ray of the lungs *preliminary* and oesophagus and in some cases also, especially if a subglottic *examination* carcinoma is suspected, of the lateral aspect of the larynx should be carried out. Auscultation of the lungs to estimate the air entry, and of the oesophagus to estimate the swallowing function, as well as the usual pharyngeal and laryngeal examinations should be made.

Anaesthesia
General

Anaesthesia may be either general or local; if a general anaesthetic is thought advisable a basal anaesthetic such as avertin, followed by the oral administration of gas and oxygen, is usually most satisfactory. If

Local

local anaesthesia is preferred, as it should usually be for bronchoscopy, a preliminary injection of morphine sulphate $\frac{1}{4}$ grain, hyoscine hydrobromide (scopolamine) $\frac{1}{120}$ grain, and atropine sulphate $\frac{1}{100}$ grain is given. For the local anaesthesia a 10 per cent solution of cocaine hydrochloride is used in the following manner: about 15 minims of this solution is sprayed on to the fauces and pharynx; then a laryngeal applicator tipped with wool is moistened in the solution and applied to the inner surface of both lips and to the base of the tongue. The applicator is passed down along the posterior pillar of the fauces into the pyriform fossa and held firmly in position for a few moments. This procedure is repeated two or three times on each side with the object of blocking the superior laryngeal nerve. The applicator is brought closely in contact with the posterior pharyngeal wall and more particularly with the laryngeal aspect of the epiglottis. The patient is then ready for examination.

Position of patient

Some surgeons prefer to have the patient sitting up on a low stool with the neck stretched forwards and the head extended; but the recumbent position is most satisfactory and comfortable, both for the patient and the surgeon. The patient lies on his back on the table with the shoulders as far as the middle of the scapula projecting over the end. The head is held by an assistant sitting on the right side with his right arm under the neck and his left hand supporting the occiput. This position of the hands enables the assistant to hold a prop in the mouth with his right hand and to extend the head at the atlanto-occipital joint for the introduction of the tube and to move the head laterally if required for bronchoscopic examination. To obviate the necessity for an assistant, several mechanical head-rests have been invented. These are adjustable, and, by various devices, allow the head to be flexed, extended, or moved laterally, so that the tube corresponds to the axis of the lumen of the passage that is under examination.
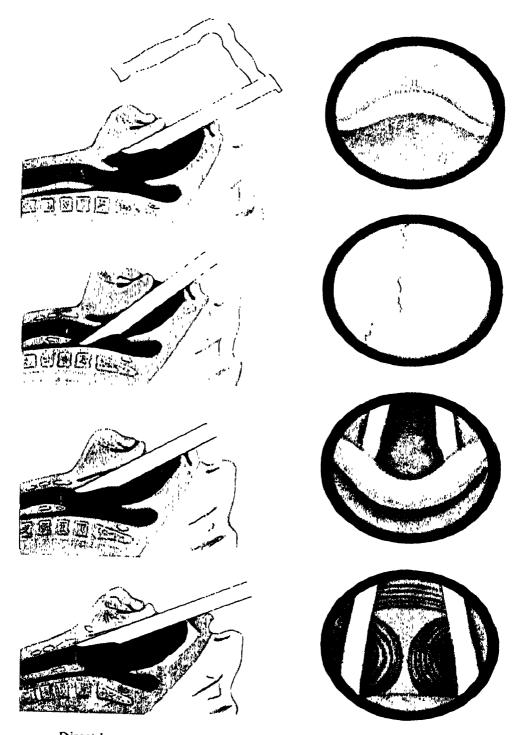
4.–DIRECT LARYNGOSCOPY

(1)—Technique

408.] The larynx cannot normally be seen by direct vision; direct laryngoscopy consists in the introduction of an illuminated tube-spatula with which the soft parts are displaced and straightened sufficiently to secure inspection of the interior of the larynx and its surrounding parts.

Introduction of instrument

After general or local anaesthesia the patient is placed in the dorsal recumbent position. The surgeon stands at the head of the patient and, holding the laryngoscope in his left hand, introduces it along the side of the tongue until, by pressing gently on the base of the tongue with the tube-spatula, the free edge of the epiglottis comes into view. The

Direct laryngoscopy. Various positions of laryngoscope and view
obtained at each

PLATE I

right hand of the surgeon retracts the patient's upper lip and protects
the incisor teeth from pressure while, at the same time, the tube-spatula
is pushed downwards. The end of the tube-spatula is slipped backwards
behind the laryngeal surface of the epiglottis as far as its base and then
the epiglottis is lifted forwards. The main pressure of the barrel of the
tube-spatula is on the base of the tongue and the upper teeth should not
be used as a fulcrum, otherwise disasters are certain. The arytenoids
and the ventricular bands are now visible. When the patient takes a deep *Appearances*
breath the true vocal cords are seen in their entire length and the inter-
arytenoid fold also comes into view. This picture of the larynx differs
from the image seen in the laryngeal mirror by indirect laryngoscopy.
In the first place, with direct laryngoscopy the posterior part of the
larynx is seen most easily and the anterior commissure with difficulty,
whereas in the mirror image the anterior commissure can usually be seen
well and the inter-arytenoid fold with some difficulty. Again, in the
mirror the true vocal cords appear as white flattened bands with a
sharp edge, whereas by direct vision with the tube-spatula they look
thick, reddish, and rounded (see Plate I).

(2)—Uses and Indications

Direct laryngoscopy is a valuable aid in the diagnosis and treatment
of many diseases of the larynx, besides forming the basis of all endo-
scopy of the respiratory passages. It is particularly useful in children
and others who will not tolerate examination with the mirror. In
children, the aetiological diagnosis of obscure cases of laryngeal stenosis
is facilitated and the removal of papillomas of the vocal cords made
possible. Papillomas may require repeated removal and it is essential
that this should be carried out without injuring the submucous tissues of
the larynx which are very delicate in a child, otherwise permanent dam-
age to the voice will ensue. Papillomatosis in children is a self-limited
disease and if the airway is maintained by repeated removal the growths
will eventually disappear.

The removal of foreign bodies which have become impacted in the *Foreign*
larynx is greatly facilitated by direct laryngoscopy, as not only can a *bodies*
better hold of the body be obtained but also rotation about the longi-
tudinal axis, often necessary for disimpaction, can only be carried out
with straight forceps.

The accurate delineation of malignant tumours or tuberculous pro- *New growths*
cesses is often possible only by direct inspection, for examination with *and*
the mirror may fail to reveal subglottic extensions or invasion of the *tuberculosis*
sinus of Morgagni; furthermore, lesions on the posterior wall are more
readily seen by the direct method, and, if necessary, galvano-caustic
puncture can be carried out more successfully and accurately. The limits
of cancer of the pyriform fossa, the aryepiglottic fold, and of the post-
cricoid region can also be defined. Small benign growths on the edge
of the vocal cords, such as haemangiomas or fibromas, can be removed
very readily, as can also singers' nodes, which must be shaved off the

cord without damaging it. The removal of small portions of tissue for biopsy is scarcely possible in many cases without direct access.

5.—DIRECT TRACHEO-BRONCHOSCOPY

(1)—Technique

Introduction of tube and appearances

409.] Direct examination of the tracheo-bronchial tree is termed tracheo-bronchoscopy or simply bronchoscopy (see Fig. 1). It is best carried out with a distally lighted tube of the Jackson type. The

FIG. 1.—Bronchoscope in position after removal of laryngoscope. Surgeon's left index retracts upper lip while other fingers protect teeth and steady tube. Assistant hands bronchoscopic forceps

patient is prepared in the same way as for direct laryngoscopy and is in the dorsal recumbent position with the head supported by an assistant or by a mechanical head-rest. The vocal cords are presented in the usual way by the direct laryngoscope held in the surgeon's left hand. The illuminated bronchoscope held in the right hand is then passed through the laryngoscope; the surgeon then transfers his eye to the bronchoscope

Vocal cords

and holds it for a moment above the vocal cords. When the cords abduct during inspiration he slips the slanted end of the bronchoscope between

Trachea

the two cords with a slightly rotatory movement. The trachea then comes into view. The slide which forms part of the barrel of the laryngoscope is pushed up and the laryngoscope is removed, thus leaving the bronchoscope through the larynx with its end free in the trachea. The further exploration of the tracheo-bronchial tree is a matter of following the lumen in its various directions. As soon as the larynx is passed the

posterior membranous wall of the trachea is presented. This usually projects a little below the cricoid cartilage and is apt to convey the false impression of a stenosis or a retro-tracheal tumour, but if the tube is displaced forwards the whole lumen of the trachea is seen. The brightness of the field of vision depends upon the degree of injection of the
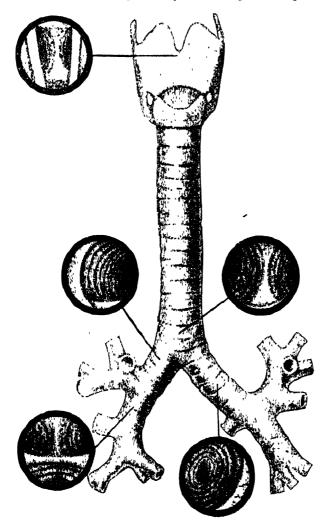
FIG. 2.—Bronchoscopy. Appearances at various levels

mucous membrane, the colour of which in different patients may vary from a yellowish pink to a dark bluish red, the latter coloration almost concealing the rings which usually are clearly marked out. If the wall is blanched by the application of a solution of adrenaline hydrochloride (1 in 1,000) the brightness is almost doubled. As the tube is carefully pushed down, the sharp white ridge of the carina which marks the bifurc- *Bifurcation* ation is seen. Recognition of this landmark should never be omitted, as sometimes it is extra-medial and, if it is not looked for, the tube may slip down unawares into the right main bronchus. When the lumen

of the right main and stem bronchus is presented a view of the lower-lobe bronchi is usually obtained; indeed, the white bifurcation ridges of the tertiary bronchi at the bottom of the lower-lobe branch may even be seen. This picture, however, changes easily, as the slightest movement of the tube causes other branches to be presented in the depths of which fresh ridges become visible (see Fig. 2).

Upper-lobe bronchus

When the lumen of the right main bronchus is presented the upper-lobe bronchus is, as a rule, concealed and it requires some displacement of the tube to bring its wall into view. Two manoeuvres facilitate this; the tube is brought to the bifurcation and then advanced from 1 to 1·5 centimetres, the head of the patient being brought to the left. Pressure against the lateral wall will generally reveal the free edge of the upper-lobe bronchus faintly protruding into the lumen. Alternatively, the tube is pushed well into the stem bronchus and then withdrawn with strong lateral displacement, when the ridge of the upper-lobe bronchus will suddenly appear in the field of vision standing out clearly against the ring markings. It is always important to see the opening of the upper-lobe bronchus lest there be a foreign body lodged in its mouth or a trickle of sputum coming down it from a focus of infection in the upper lobe. In this case the mucosa at the orifice will usually be seen to be red and pouting.

Right stem bronchus

After passing the vertical spur of the right upper-lobe bronchus the tube enters the right stem bronchus. The head is lowered and the horizontal ridge of the middle-lobe bronchus on the anterior wall will be seen.

Middle-lobe bronchus

By further manipulation the tube is brought into line with the axis of the middle-lobe bronchus and this is examined. As the lower-lobe bronchus passes somewhat dorsally the head must be raised a little until

Lower-lobe bronchi

its axis is brought into line. Careful inspection will then reveal the openings of the branches that serve the lower lobe.

Left bronchial tree

On examination of the left bronchial tree the sharper angle of origin (75° to the tracheal axis) of the main bronchus is evident and its length, which is double that of the right, is noted. The tube is advanced somewhat and pressure on the outer wall with the end of the tube will reveal the oblique spur of the upper-lobe bronchus. As the head is drawn strongly to the right, and a little more lateral pressure is exerted on the lateral wall, the upper-lobe bronchus comes into view. For the examination of the lower-lobe bronchus, as on the right side, the head must be raised and retained in the lateral position. The branch bronchi will then come into view.

(2)—Uses and Indications

Bronchoscopy was formerly chiefly concerned with foreign bodies in the air passages and their extraction, but in recent years it has developed a wide range of usefulness in the diagnosis and treatment of pulmonary disease. Its value is recognized not only as an aid to the diagnosis of difficult cases but also as providing an efficient form of treatment in

the simpler ones. Among conditions that require bronchoscopy may be mentioned: (*a*) any form of bronchial obstruction; (*b*) bronchiectasis (early cases and late bilateral cases); (*c*) acute lung abscess following tonsillectomy or anaesthesia; (*d*) chronic lung abscess; (*e*) post-operative atelectasis (massive collapse); (*f*) unexplained haemoptysis; (*g*) unexplained dyspnoea; (*h*) obscure pulmonary disease; (*i*) chronic cough.

(*a*) *Bronchial Obstruction*

The commonest cause of bronchial obstruction is an inhaled foreign *Foreign* body. As foreign bodies may be of all sizes, shapes, and consistencies *bodies* the conditions to which they give rise when lodged in a bronchus vary widely and depend not only on the degree to which the bronchial tree is obstructed but also on the duration of the obstruction and the capacity of the foreign body to swell and so cause increased obstruction or to produce ulceration of the mucosa with subsequent formation of scar tissue.

The size of the foreign body in relation to the age of the patient is very important, since on the site of impaction depends the area of lung that may be affected.

Non-opaque foreign bodies, such as peas and beans, which are not *Non-opaque* infrequently aspirated by children, swell up rapidly, causing acute *foreign bodies* inflammation and oedema of the mucosa and thence considerable dyspnoea. If complete occlusion of one bronchus is so caused, total atelectasis of the lung may occur, and this has not infrequently been mistaken for some other condition such as empyema. The fact that complete atelectasis may be caused when a bronchus is obstructed should be remembered when any attempt at extraction is made, for unless the surgeon is on his guard against it a fatality may follow. This was illustrated by a case in Killian's clinic many years ago:

> A child had inhaled a small bean which swelled up and occluded the main bronchus. The extraction was not considered likely to offer any particular difficulty, and the bean was readily located by bronchoscopy and seized with the appropriate forceps. Unfortunately, just as the bean was being drawn through the larynx it slipped or broke from the forceps and was inhaled into the healthy bronchus. As one lung was completely collapsed and the other one was immediately put out of action, the child died of suffocation before it was possible to recover the bean.

Obstruction in the tracheo-bronchial tree is often caused by disease, *New growths* and bronchoscopy is often essential in order that the disease may be *of bronchus* recognized and treated. Among the most common conditions in this connexion are malignant growths. Any of the ordinary non-malignant growths ·e.g. fibromas, lipomas, haemangiomas, and adenomas—may occur in the trachea and bronchi, but adenomas seem to be by far the most common. Taking all bronchial neoplasms together, the non-malignant growths provide only about 5 per cent, the malignant growths being mainly responsible for bronchial obstruction and its signs and symptoms. These signs are caused (1) directly by the tumour

(haemoptysis, cough, asthmatoid wheeze), and (2) secondarily by broncho-stenosis (atelectasis, pneumonia, bronchiectasis).

New growths of lung
The incidence of carcinoma of the lung is increasing; but part of the increase is only apparent, many more cases being diagnosed as the signs and symptoms are becoming better understood. X ray technique has improved and examination of the sputum for particles of growth by the wet-film method of Dudgeon and Wrigley has afforded additional help. Most important of all, however, is the more general use of bronchoscopy, for by this means not only can the early pathological changes in the mucosa be seen but portions of tissue can be removed for biopsy. Furthermore, primary carcinoma of the lung, being broncho genic in 85 to 90 per cent of cases and usually situated near the hilum of the lung, may readily be recognized, inspected, and, if treatment is possible, dealt with by bronchoscopic methods. The number of cases in which these have established the diagnosis is rapidly increasing, and many cases are now reported in which carcinomas have been removed from the bronchi and the patients have remained alive and well four *New growths of mediastinum* or more years afterwards. Again, bronchoscopy can show whether obstruction of a bronchus is due to a neoplasm within the lumen or to pressure from without by a mediastinal or other growth. In these conditions the clinical signs and X-ray appearances are very similar, and the bronchial neoplasm in its early stages is often firm and nodular, so that no particles are likely to appear in the sputum.

Other causes of bronchial obstruction
Other causes of bronchial obstruction are swelling of the mucosa, or granulomas due to local inflammatory conditions, and stenoses of the interior of the tracheo-bronchial tree resulting from a cicatricial contraction following syphilitic, tuberculous, or traumatic lesions. Compression of the trachea or bronchi from without may be caused by goitres, aneurysms, mediastinal glands (malignant, tuberculous, or lymphadenomatous), or even by a dilated left auricle.

(b) Bronchiectasis

Causes
Bronchiectasis often originates with the acute infectious diseases of childhood, such as whooping cough, measles, scarlet fever, and diphtheria (see Vol. II, p. 682). Its early recognition and the institution of *Associated conditions* bronchoscopic treatment have given a high percentage of cures. The association of accessory sinus suppuration is well known, and after treatment of the sinus several bronchoscopic treatments are necessary before the condition clears up. The possibility that a bronchiectasis, particularly if unilateral, may be due to a foreign body must not be overlooked and, in view of the frequency with which an unsuspected foreign body is found, bronchoscopy should be undertaken in all cases. After removal of the foreign body fully 90 per cent of the cases clear up completely.

Broncho-scopic aspiration
In bronchiectasis not due to a foreign body bronchoscopic aspiration is an important therapeutic measure. In bronchiectatic cavities there is little if any ciliary action and, although the compression of the lung during forced coughing may drive the secretion from the periphery of

the lung, ciliary action plays the chief part in the upward drainage. If this is absent, stagnation of secretion is apt to occur. Gravity to some extent helps the drainage, and postural coughing may be of some help; but when the secretion is coughed up there is often a contraction of the bronchi above the cavity which is consequently not properly emptied. It is of the utmost importance that infected secretion should not be allowed to stagnate in the cavities. Bronchoscopic aspiration, lavage if the secretion is very viscid, and the application of silver nitrate to the mucosa of the dilated bronchi will rapidly improve the condition.

(c) Acute Lung Abscess

These abscesses may follow tonsillectomy or operations performed in *Pathogenesis* the presence of septic teeth. The pathology is rather obscure and it is doubtful whether the path of infection is by the lymph channels from the field of operation to the veins and thence by a septic embolus to the lungs or by aspiration. But, whatever the origin, bronchoscopy and aspiration should be performed when cough and expectoration start after tonsillectomy.

(d) Chronic Lung Abscess

Chronic lung abscess may be due to many causes. One of the most *Pathogenesis* important is an unsuspected foreign body. In a case under my observation bronchoscopy showed a rabbit's vertebra impacted in the right main bronchus; it had certainly been there for more than six months and its extraction followed by aspirations resulted in a cure. This case was complicated by stenosis of the bronchus due to cicatricial contraction which was satisfactorily dilated with a flexible metal tube inserted bronchoscopically.

Other causes of chronic lung abscess are pieces of tooth-filling that have been inspired. Exploratory bronchoscopy may enable the foreign body to be seen and extracted, and six or eight subsequent aspirations will probably result in a complete cure. Once the foreign body has been removed and bronchoscopic aspiration carried out so as to prevent the stagnation of secretion, it is remarkable how quickly the patient gets well. Other causes of lung abscess that have been found and treated bronchoscopically are those following pneumonia or influenza. In such cases a bronchus may be partially occluded by a granulation or by thickened velvety mucosa with secretion retained behind it. Removal of granulations, dilatation of the bronchus, and application of silver nitrate to the swollen mucosa will soon result in resolution.

(e) Massive Collapse of the Lung (Post-Operative Atelectasis)

Aspiration by bronchoscopy of viscid secretion blocking and thus causing collapse of the lung enables it to expand again (see LUNG DISEASES).

(f) Unexplained Haemoptysis

In the large majority of cases haemoptysis is caused by pulmonary tuberculosis, but there are always a number of cases in the diagnosis of which bronchoscopy is indispensable. Among the causes of haemoptysis that may be discovered by this means are varices of the bronchial or tracheal mucosa, benign growths, malignant growths, granulomas of inflammatory origin, or the dry bronchiectasis described by Bezançon and Weil. In some cases of tracheal varix the haemoptysis may be alarming and the patient may bring up as much as a pint of blood a day. This is usually of sudden onset and may occur equally at rest or on exertion. The blood is usually bright and is never frothy. Bronchoscopy shows that the varix is usually on the anterior tracheal wall just below the vocal cords, but it may also occur on the posterior wall near the bifurcation or elsewhere. The varix may be clearly defined or there may be a diffuse hyperaemia of the mucosa. Varices are very rare in the bronchi. When they are diagnosed, cauterization with trichloracetic acid or chromic acid fused on a silver wire is usually most effective.

Causes

Tracheal varix

(g) Unexplained Dyspnoea

Unexplained dyspnoea, more particularly an asthmatic wheeze such as is usually associated with a foreign body in the bronchus, is a definite indication for bronchoscopy. In some cases the dyspnoea is due to a bronchial neoplasm. In a case reported by Wessler-Rabin, change of position produced an alarming dyspnoea and this was shown to be due to a small almost pedunculated bronchial carcinoma which altered its position and gave rise to a ball-valve obstruction. The asthmatoid wheeze first described by Chevalier Jackson is produced by obstructive narrowing of some part of the lumen of the trachea or bronchus, by a foreign body, a neoplasm, or thick tenacious secretion retained by defective ciliary movement.

(h) Obscure Pulmonary Disease

Obscure pulmonary disease is often investigated by the injection of iodized oil (lipiodol, neo-hydriol) into the tracheo-bronchial tree through the thyrohyoid membrane, but in some cases there is difficulty in getting the periphery of the lung satisfactorily mapped out. In such cases the iodized oil is best introduced bronchoscopically, because the area of the lung or tracheo-bronchial tree that it is desired to study can be aspirated free from obstructing secretion and the iodized oil is thus enabled to penetrate further.

(i) Chronic Cough

Chronic cough with or without sputum, if not readily accounted for by some such condition as tuberculosis, pulmonary abscess, foreign body, bronchiectasis, malignant disease, or heart disease is usually designated as chronic bronchitis. These cases of unexplained cough may

have some underlying cause which is not due to disease in the nose, throat, or sinuses and which is not revealed by the ordinary methods of examination. Bronchoscopy has often in such cases revealed a bronchi-ectasis or broncho-stenosis, and the aspiration of secretions followed by the instillation of iodized oil through the bronchoscope has in many cases effected complete disappearance of cough and expectoration, marked subjective improvement, and gain in weight.

(3)—Contra-Indications

There is no real contra-indication to bronchoscopy, more particularly if the examination is a matter of urgency. But cases of aneurysm, uncompensated heart disease, and advanced arteriosclerosis should if possible be avoided. Some consider that bronchoscopy is harmful in cases of pulmonary tuberculosis, but I have never found this to be the case and, indeed, it may be of considerable value.

6.—OESOPHAGOSCOPY

410.] Oesophagoscopy, no less than bronchoscopy, presupposes an exact knowledge of the normal anatomical, topographical, and functional characteristics of the patient to be examined. The conditions, however, as regards the method of examination are much simpler than in the complicated air passages.

(1)—Anatomy and Action of Oesophagus

The oesophagus (see Fig. 3) is a thin-walled tube which is easily distensible owing to the elasticity of its walls. It begins at the lower border of the cricoid cartilage and, passing through the oesophageal opening in the diaphragm, enters the stomach at the cardia. It passes first downwards, backwards, and slightly to the left, and then behind the arch of the aorta and the left bronchus, and turns slightly forwards and then to the left to the diaphragmatic opening. As it passes through the diaphragm it turns much more obliquely to the left.
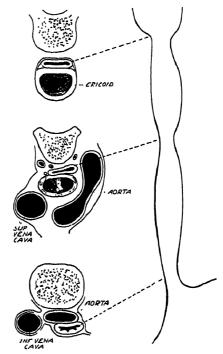
FIG. 3.—Anatomical relations of oesophagus at main constrictions

The lumen of the oesophagus shows four constrictions (see Figs. 3 and 4): (a) the cricopharyngeal opposite the sixth cervical vertebra, (b) where

the arch of the aorta crosses it at the level of the fourth dorsal vertebra, (c) below this at the level of the fifth dorsal vertebra, where the left bronchus covers it, and (d) at the oesophageal opening in the diaphragm opposite the tenth dorsal vertebra. The cervical and diaphragmatic narrowings are more marked than those in the middle of the tube.

The average measurements of the oesophagus are:

FROM TEETH IN DIRECT LINE

		TO MOUTH OF OESOPHAGUS	TO LEVEL OF LEFT BRONCHUS	TO CARDIA
Adult male	–	16 cm.	27 cm.	40 cm.
Child of ten	–	12 cm.	20 cm.	27 cm.
At birth –	–	7 cm.	13 cm.	18 cm.

The approximate distances are shown diagramatically in Fig. 4.

Mechanism of swallowing

The act of swallowing takes place in two stages. In the first the bolus of food is pushed by the tongue through the fauces, the pharynx shapes itself like a funnel, and the nasopharynx is shut off by elevation of the soft palate, and contraction of the posterior palatine arches and the superior constrictor muscle. The larynx is then drawn forcibly upwards and forwards towards the base of the tongue by the contraction of the thyrohyoid muscle and, at the same time, moved forwards away from the vertebral column by the action of the muscles of the floor of the mouth (geniohyoid and mylohyoid and anterior belly of digastric). At this moment the bolus of food passes backwards over the larynx and drops into the mouth of the oesophagus which opens reflexly to receive it. This stage may be called the bucco-pharyngeal stage, and the further progress of the bolus the oesophageal stage. This also

FIG. 4.—Distances of main constrictions of oesophagus from teeth in the direct line

is of the nature of progressive peristaltic contraction, the rapidity of which is far greater in the upper and striated portion of the muscular tube than in the lower two-thirds.

Normally the upper end of the oesophagus is closed by the crico-pharyngeus muscle pulling the oesophagus to the back of the cricoid, while the lower end is closed by the crura of the diaphragm. During

deglutition the normal tonic contraction of the oesophageal openings
is reflexly relaxed to permit the bolus to pass.

(2)—Technique

The position of the patient for oesophagoscopy is the same as that *Position of*
for bronchoscopy—namely, lying on his back with the head and shoulders *patient*
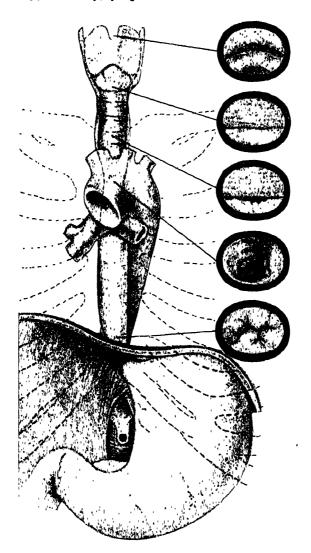
FIG. 5.—Oesophagoscopy. Appearances at various levels

over the end of the table, the head being supported by an assistant or
by a mechanical head-rest. At first the head is slightly raised but
somewhat extended at the atlanto-occipital joint. The surgeon, standing
at the head of the table, holds the oesophagoscope in his right hand,
and with his left hand protects the patient's upper lip and teeth. The *Introduction*
of tube and
tube is then passed backwards to the posterior pharyngeal wall and *appearances*

then downwards along its right postero-lateral aspect until, passing the right arytenoid, it reaches the posterior part of the right sinus pyriformis. The cricopharyngeal fold on the posterior wall of the deep pharynx then comes into view. This is just above the sphincter which guards the mouth of the gullet and which is in a state of tonic contraction. As the end of the tube is lifted forwards by the left thumb and pushed slightly downwards, gentle pressure of the end of the tube causes the sphincter to relax and the lumen to appear. This stage should on no account be hurried, as the sphincter may not dilate immediately, but the more accurately and quickly the tube is introduced the less likely is there to be any difficulty. As the tube enters the gullet the head is lowered and drawn to the right, so that the tube lies in the axis of the thoracic portion of the gullet. The pulsation of the aorta is noted on the left antero-lateral wall and, as the lumen of the gullet is widely open, the tube is pushed downwards and the oesophageal opening in the diaphragm looked for; this usually appears as an oblique slit or sometimes as a rosette. Moderate pressure enables the tube to pass into the abdominal oesophagus and, without any noticeable constriction at the cardia, the change of colour of the mucosa, the gastric rugae, and a gush of gastric secretion show that the tube has reached the stomach. In the thoracic part of the gullet respiratory movements may be observed; they consist of dilatation of the lumen during inspiration and are due to the negative intrathoracic pressure; they do not occur at the crico-pharyngeal level or at that of the diaphragmatic opening. The appearances at various levels are shown in Fig. 5.

(3)—Uses and Indications

Foreign bodies
Oesophagoscopy in former years achieved its most brilliant successes in the extraction of swallowed foreign bodies. In this it still remains of paramount importance, but more recently it has also been used for the diagnosis and treatment of many forms of oesophageal disease.

Symptoms
The symptoms to which a foreign body may give rise are very variable, but, when it is lodged in the upper part, there is usually a sensation of something sticking, and this is more marked if the object is pointed, such as a sharp bone, and may amount to actual pain when the act of swallowing is attempted; often dysphagia or odynophagia is the most prominent feature. Occasionally there are symptoms referable to the air passages, such as dyspnoea, wheezing, or cough. These may be due to compression of the air passages from behind or to the trickling of secretion into the larynx and bronchi. In perforation of the cervical portion of the gullet by a sharp-pointed body there may be surgical emphysema in the neck. The history of the foreign body is usually clear, and, when its probable nature has been ascertained, X-ray examination before the fluorescent screen should be carried out both in the antero-posterior and lateral positions; and the act of swallowing of barium sulphate emulsion and of barium porridge should be observed, more particularly if a non-opaque foreign body is suspected. When the site of impaction has

X-ray examination

been ascertained, oesophagoscopy should be undertaken and the surgeon *Findings on* should have a complete set of bronchoscopic as well as oesophageal *oesophago-scopy* tubes and instruments available in case of need. The great majority of foreign bodies are arrested at the upper end of the gullet just below the cricopharyngeal fold. In this situation coins stick transversely and if the patient is not seen soon after the accident the cricopharyngeal fold may be swollen and hide the upper edge of the coin. The oesophagoscope then tends to override it. The presence of small masses of food above the foreign body or of lacerated mucosa may render its recognition very difficult. When, however, the foreign body is definitely located in this situation, extraction with suitable forceps is not usually difficult, but every foreign-body problem should be approached methodically and without undue haste. The second most common site at which foreign bodies may stick is at the bifurcation of the trachea. Large and sharp-pointed foreign bodies are often arrested in the middle of the gullet.

As foreign bodies may vary so widely the problem of their extraction often presents great difficulties. Among the most troublesome are multiple sharp-pointed objects such as a bunch of open safety-pins with the points uppermost, staples, irregular and pointed bones, or brooches, because if they have not already pierced the oesophageal wall a tear may be caused unless they are disimpacted with great care. A bone lying across the oesophagus should be seized near one end so as to swing it into the long axis of the oesophagus.

For symptoms of disease of the oesophagus, including stenoses (cicatricial, congenital, compression, malignant, or functional), diverticula (pulsion or traction), ulcers, acute and chronic inflammatory conditions, and paralyses, see OESOPHAGUS, DISEASES.

7.—GASTROSCOPY

411.] During oesophagoscopy of the lower end of the gullet the tube is *Rigid tubes* often pushed into the cardiac end of the stomach. Examination of more distant portions of the stomach requires a longer tube which is introduced in precisely the same way as the oesophagoscope. The rigid gastroscopic tube can be closed with a window plug at the proximal end when it is thought advisable to inflate the stomach. The oblique passage of the gullet through the diaphragm and the forward curve of the pars diaphragmatica and the pars abdominalis cause the rigid gastroscope, when passed into the distended stomach, to lie close to the posterior wall or in the angle between the posterior wall and the lesser curvature. This position restricts the field of vision, and, for this reason, experiments were made with semi-flexible gastroscopes incorporating a lens system so that the gastric mucous membrane could be seen through *Semi-flexible* a window situated in the lateral wall of the tube near the tip. The Wolf- *tubes* Schindler gastroscope provides the most satisfactory optical system and is the one usually employed. The disadvantage of the semi-flexible

gastroscope from the endoscopic point of view is that it must be passed blindly and thus violates the chief principle of endoscopic examination, namely that every step should be carried out under direct vision.

Insertion of instrument   If, however, an oesophagoscopic examination shows the gullet to be free from disease the careful passage of the semi-flexible gastroscope is not attended with danger. Cocaine anaesthesia, as for other endoscopic examinations, is sufficient, and the stomach should always be washed out as a preliminary measure. As the gastroscope can only be rotated in and out of the stomach and cannot be moved sideways, it is necessary, in order that the greatest possible area of mucous membrane can come into view, so to arrange the position of the patient that he may be moved as it were round the gastroscope. The patient lies in the left lateral position, the left leg being drawn up and flexed and the upper one extended. The head is supported by an assistant and slightly extended at the atlanto-occipital joint. The passage of the gastroscope does not present any unusual difficulty and with the co-operation of the patient it can practically be swallowed. On no account should any force be used. When the gastroscope is in position the stomach should be *Appearances*   moderately inflated. Gastric endoscopy gives information about the general size and shape of the viscus, the degree of activity of the peristalsis, the amount and consistency of the mucus, the colour of the mucous membrane, the appearance of the vessels, the sites of haemorrhages, and the presence of hyperplasias, atrophies, and erosions.

Uses and indications   Gastroscopy does not detract from the value of radiology but is complementary to it. In doubtful cases of carcinoma, in which the radiological findings are indefinite, gastroscopy may be a decisive factor in diagnosis, determining the decision to perform or avoid an operation. Cases of doubtful gastro-jejunal ulcer have been confirmed, and unsatisfactory symptoms persisting after gastro-enterostomy have been explained by direct inspection of the gastric mucous membrane.

Gastroscopy should not be carried out as a routine measure but only in cases in which there is a definite indication for its employment.

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ENDOSCOPY OF THE URINARY TRACT

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Reference may also be made to the following titles:

BLADDER DISEASES   KIDNEY, SURGICAL DISEASES

1.–URETHROSCOPY

412.] Urethroscopy is very rarely needed for examination of the female urethra. In the male, however, it is such a comparatively common investigation that the following considerations deal almost entirely with the male urethra, which for purposes of inspection is arbitrarily divided into two parts—anterior and posterior. The anterior urethra corresponds to the spongy or penile portion and extends from the external urinary meatus to its continuation in the membranous urethra; the posterior urethra extends to the internal urinary meatus of the bladder.

(1)—Selection of Instruments

The instruments designed for urethral endoscopy are of two main types: (*a*) those with direct vision, and (*b*) those with indirect vision with a telescope. An instrument with direct vision, eminently suitable for inspection of the anterior urethra, has been developed by Wyndham Powell, the most satisfactory form being the aero-urethroscope. The Wyndham Powell or Swift Joly modification has an external projected lighting system which requires focusing and gives the best view of the urethra. Harrison's instrument has an internal distal end light, does not require focusing, and is more useful as an operating instrument.

The Swift Joly aero-urethroscope which is used at St. Peter's Hospital *Swift Joly* consists of two parts: (*a*) a series of straight cannulae with obturators *aero-* from 18 to 28 Charrière size for introduction into the urethra, and (*b*) *urethroscope* the combined lighting and optical system to be attached to the distal end of the cannula after the latter's insertion, the obturator having been removed. The fitting of the two parts is air-tight and there is a nozzle with tap on the side of the viewing end to which bellows can be attached and through which the urethra can be dilated to the required degree.

For examination of the posterior urethra, a cysto-urethroscope is the *Cysto-* instrument of choice. It is easier to introduce and is less likely to cause *urethroscope* trauma. A constant flow of irrigating fluid provides dilatation of the posterior urethra, and facilitates both to-and-fro and rotary movements of the instrument. There are many models, Buerger's and Lewin's being probably the commonest in use. In brief the instrument consists of (*a*) a sheath fitted with two flushing stopcocks, and with a straight or slightly curved beak, and (*b*) a combined optical and lighting system for introduction along this sheath, the lamp and prism window being so placed as to obtain the full advantage of light and vision.

(2)—Anterior Urethroscopy
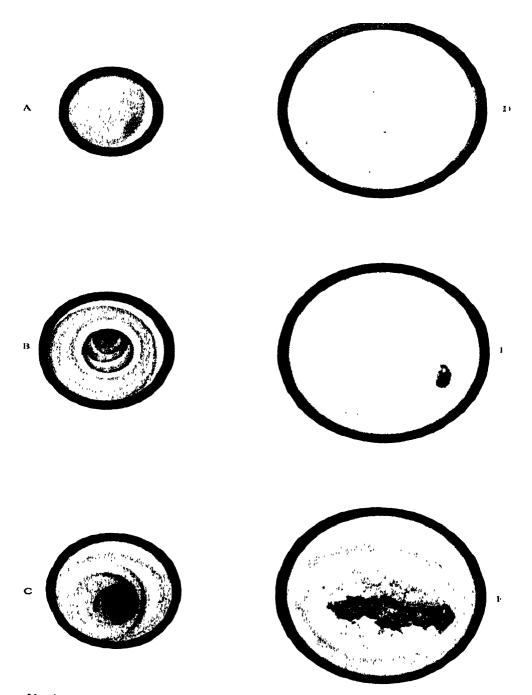
(*a*) *Examination*

The patient passes urine, and is then placed on his back with the thighs slightly abducted, on a couch or table. The external meatus and glans penis are cleaned with 70 per cent alcohol or mercuric oxycyanide solution 1 in 4,000. The examination, although uncomfortable, should

*Introduction
of instrument*

never be painful, and a local anaesthetic is unnecessary. The urethra should not be irrigated before this examination. The instrument is tested for lighting and focus and the bellows are attached. A cannula which does not fit too tightly is selected and is sterilized by boiling. The penis is lifted up, the glans being held between the thumb and index finger of the left hand. The cannula is lubricated and introduced into the external urinary meatus; it should pass quite easily by its own weight, and no force should be used in its introduction. If an obstruction is felt, the obturator should be removed. A sterile swab on a probe is now introduced and the urethra is mopped dry of lubricant. This must be done very gently, and should any blood be seen on the swab the cannula must be removed and the examination postponed for a week. Fatalities from air embolism have followed neglect of this danger signal, especially when there is a laceration in the region of a hard stricture. When all goes well, the optical system of the urethroscope is now attached to the cannula, the left hand steadying the penis in the meantime. By gently squeezing the bellows the urethra is now dilated and inspection begun.

(b) *Appearance of Normal Anterior Urethra*

It will probably be necessary to insert the cannula a little further under vision in order to reach the most distal part of the anterior urethra. The opening into the membranous urethra will be seen as a dark spot, pin-head in size with radial striation from folds of mucous membrane, situated on the anterior wall just above the centre of the field. The latter will be formed by the posterior recess of the spongy urethra. The cannula is now gradually withdrawn, the urethra being kept dilated, if necessary by a little further pressure on the bellows; at the same time the thumb and index finger of the left hand prevent as far as possible the exit of air along the side of the cannula at the external urinary meatus. A continuous inspection of the urethral wall is made as the instrument is withdrawn. The dilatation of the first part of the bulbous urethra will be noticed for about one and a quarter inches. On the floor or posterior wall of this part, about one inch from the opening into the membranous urethra, the openings of the Cowper's (bulbo-urethral) ducts can be seen, one on either side of the mid-line. They are usually, but not always, symmetrical, the left sometimes opening a little further forward than the right. The mucous membrane appears a pale pink colour with a smooth glistening surface. The walls are seen to be symmetrical and quite mobile with the calibre of the canal more or less circular. Several small pin-head openings can be seen on the roof of the urethra; these are the lacunae of Morgagni, leading into blind recesses. In the distal inch of the urethra in the region of the glans, there is another dilatation of the canal—the fossa navicularis—and in the roof of this fossa, near its commencement, is a larger lacuna called the lacuna magna or Guerin's valve. Normally the openings of the ducts of Littré's glands are too small to be seen.

Urethroscopy. A. Numerous areas of soft infiltration in anterior urethra. B. Early stricture in anterior urethra. C. Three papillomas in anterior urethra. Cystoscopy. D. Vesical haemorrhage due to arteriosclerosis. Note bleeding points and prominent arteries. Patient was aged 41 and died of cerebral haemorrhage a few months after this drawing was made. E. Stone presenting at right ureteral orifice and causing bulge in intramural portion of duct. F. Stone exposed by division of wall of ureter with endothermy needle

PLATE II

(c) *Indications*

1. As a test for cure after urethritis.
2. When acute urethritis has been treated for 5 to 6 weeks without resolution.
3. Repeated difficulty in instrumentation when the presence of a false passage is suspected.
4. Haemorrhage from the penis, not associated with micturition.
5. Foreign bodies in the urethra.

The majority of pathological lesions of the anterior urethra result from *Pathological* urethritis. Gonococcal and non-gonococcal lesions present the same *conditions* urethroscopic picture and fall into two main categories: soft infiltration and hard infiltration.

Soft infiltration accompanies and results from acute inflammation. It is *Soft* an infiltration of the submucosa with round cells and an increased *infiltration* vascularity of the part. The appearance, as seen through the urethroscope, is that of localized areas of turgidity with normal mucous membrane intervening, situated mainly on the roof and lateral walls. If examined without air distension these areas resemble prolapsed haemorrhoids and bleed easily. The lesions are seldom seen if urethroscopy is delayed, as it should be, until the fifth or sixth week. At a later stage small areas varying in size from a pin's head to that of a lentil are seen with the mucous membrane standing out redder than normal (see Plate II, A). Later still these areas become pale and develop a gelatinous appearance. They can be seen better in profile when their outline is thrown up by the light shining down into the darker area of the deeper urethra. Their number varies from one or two up to the severe cases in which a large part of the mucous membrane is studded with them.

In all cases of soft infiltration the glands of Littré are infected, and in the early stages the pouting orifice of their ducts, often blocked by a plug of muco-pus, can be seen. Occasionally a small Littré abscess may also be observed.

Hard infiltration is due to connective-tissue formation following *Hard* untreated exudative cellular formation. The urethroscopic appearance is *infiltration* that of localized pallor of the mucous membrane with fixity of the wall of the urethra. In early cases resistance may be felt to the passage of the instrument and the wall will be seen to be fixed when air dilatation is attempted (see Plate II, B). In the later cases when a definite stricture *Stricture* has occurred it may prevent the passage of the instrument. The obstructing stricture can be readily seen as a small opening, often eccentric, in the central field, usually circular with a pale white or greyish circumference standing out against the blackness of the deeper urethra. A common position is well down in the bulbous urethra, and the posterior recess of this part is the commonest site for occurrence of a false passage. The region of the opening into the membranous urethra must be carefully examined, as this is the only position where it is possible to overlook a stricture. Other lesions which may be seen in the anterior

urethra are cystic dilatation of one or both of the ducts of Cowper. A rare condition is a papilloma (see Plate II, c). When it occurs in the anterior urethra it is usually at the fossa navicularis and can be seen at the external urinary meatus; it is rarely observed in other parts of the anterior urethra. Epithelioma of the urethra is very uncommon, as is also a naevoid condition which may be a source of bleeding.

On completion of the anterior urethroscopy a Janet irrigation should be given, using a solution of mercuric oxycyanide, 1 in 8,000.

(3)—Posterior Urethroscopy

(a) Examination

Local anaesthesia

Some form of anaesthesia is usually necessary—either local, low spinal, or general. For local anaesthesia a solution of procaine hydrochloride (novocain) 5 per cent is suitable; or the following solution:

Cocaine hydrochloride	0·5 gram
Sodium bicarbonate	0·5 gram
Chlorbutol	0·25 gram
Distilled water	to 100 c.c.

Method

The glans and external urinary meatus are cleaned with antiseptic; 10 c.c. of the anaesthetic solution are syringed into the urethra. The urethra near the meatus is compressed by the thumb and index finger of the left hand and the solution is then milked into the posterior urethra with the right hand. A further 10 c.c. of solution are now introduced into the anterior urethra. A penile clamp is applied and the patient left for ten minutes.

Introduction of instrument

The patient is placed in a modified lithotomy position and the cysto-urethroscope is introduced; it slips in quite easily as far as the membranous urethra. The outer end of the instrument should then be slowly and gently depressed, when the beak will slip into the posterior urethra and thence into the bladder. The latter should now be emptied and if necessary washed clear. The operator sits facing the eyepiece and continuous irrigation is begun.

(b) Appearance of Normal Posterior Urethra

The cysto-urethroscope is gradually withdrawn until the vesical sphincter appears. This is seen as a circular rim with the mucous membrane coloured a deeper red than that of the trigone of the bladder. The prostatic urethra is now entered and inspected. On the floor or posterior wall of the first part will be seen several markings or folds of mucous membrane, corresponding to those on the trigone. These folds converge to meet at a small depression in the first part of the prostatic urethra, the fossula prostatica. There are usually several vessels running longitudinally from the sphincteric rim which also converge at the fossula. Just distal to the latter in the mid-line of the floor is the beginning of the verumontanum or crista urethralis, a smooth rounded eminence covered by mucous membrane, paler than that of the roof

and walls of the prostatic urethra; it shows a proximal gradual slope
(the declive), a central rounded prominence (the summit), and a distal
sharper slope (the acclivity). The size of the verumontanum varies greatly
as also does its shape. Just distal to the summit is the opening of the
uterus masculinus, which may be quite large and gaping, slit-like, or a
mere umbilication. Symmetrically placed on either side, and 2 to 3 mm.
from this and from each other, are the openings of the ejaculatory
ducts. They can usually, but not always, be seen, and when all these
openings are visible they form the angles of an equilateral triangle. On
either side of the verumontanum is a shallow trough—the prostatic
sinus. The majority of the prostatic ducts open into these troughs and
occasionally one or more of the openings can be seen.

The mucous membrane of the prostatic urethra is smooth and glisten-
ing and is darker red in colour than that of the anterior urethra. The
roof and sides do not present anything of importance.

(c) Indications

(1) Vesical neck obstruction, when a simple cystoscopy has not
revealed the cause.

(2) Haematuria at the beginning of micturition, when a cause is not
found in the bladder.

(3) Bladder papillomas of severe degree or long duration.

(4) Persisting posterior urethritis.

The frequency of lesions of the posterior urethra is doubted by many *Pathological*
urologists. It is probable that long-continued inflammation of this part *lesions*
will leave some mark, but on the other hand the lesions which may
result from a posterior urethral infection do not appear to be of much
significance. Scarring in the region of the verumontanum and its open-
ings is probably the commonest sequela. In the presence of an infection
there is oedema of the mucous membrane with bulbous knobs resembling
small cysts. It is often difficult to differentiate a pathological lesion from
trauma following the passage of the instrument. Enlargement, from
whatever cause, of the prostate gland in the transverse plane can be seen
only with the cysto-urethroscope, and is shown as a rounded bulge on
the lateral walls. A false passage through the prostate, commonest in
the roof, can be easily seen. It may be possible to see the obstructing
folds in a case of congenital urethral valve. Papilloma occurs in the
posterior urethra much more often than in the anterior, but it is not
common. It usually occurs laterally to the prostatic sinus.

2.–CYSTOSCOPY

413.] Before the introduction of the cystoscope by Max Nitze (1876), *Historical*
diagnosis of disease of the urinary tract rested on signs and symptoms
only and, as many lesions first give rise to painless haematuria, it is
obvious how great were the difficulties of clinical diagnosis in the last

century. A reliable source of illumination for this new instrument was not available until Edison's invention of the incandescent lamp in 1886, and in consequence until this date cystoscopy made little progress.

The problem of obtaining a clear medium within the bladder by the use of catheter lavage before the insertion of the cystoscope was solved three years later by the introduction of the first irrigating cystoscope by M. B. Berkeley Hill, surgeon to University College Hospital. Further developments soon followed, and in 1893 G. Brown described catheter ization of the ureters with the aid of a cystoscope having a direct vision telescope. From this year until 1914 improvements in the optical system and the electric lamp made this instrument still more valuable in the diagnosis of urinary diseases.

Until the outbreak of the Great War, Germany was the only country to produce cystoscopes, but in 1920 R. Schranz, at the 88th Meeting of the British Medical Association, exhibited the first British-made cysto- scope. Since then the cystoscope has been so improved that the whole instrument can now be boiled, and diathermy can be applied to the anterior wall of the bladder by the aid of a retrograde telescope.

(1)—Selection of Instruments

A cystoscope has two uses, first for diagnosis, and secondly for treat- ment. The following points must be borne in mind when the practitioner is considering its purchase. The whole instrument must be easily steril-

Instruments for examination ized, preferably by boiling. When it is needed for examination of the bladder only, its calibre should be between 18 and 20 Charrière size, for the smaller it is the less damage will be done to the urethral mucosa during its insertion. On the other hand the novice is at a disadvantage when the field of vision is very narrow, and for all practical purposes this is in proportion to the size of the instrument. In the early stages of apprenticeship he should use the telescope with a wide field. This is particularly necessary when he is learning to find the ureteric orifices and to pass a ureteric catheter.

For treatment For treatment a much larger cystoscope is needed. There are two British-made patterns in use which fulfil all the requirements for the treatment of lesions in and around the ureteric orifices and for the passage of a large diathermy electrode. One has been designed by Swift Joly and the other by Winsbury White. Both are of very large calibre and necessitate either general or local anaesthesia.

The cystoscope, being in many respects a delicate instrument, must be handled with care. The telescope consists of numerous tiny magnifying glasses and at its bladder end a prism and a minute glass window. The slightest knock may disturb the alignment of either the prism or one of the magnifying glasses, with the result that the image is blurred.

For use in children In recent years considerable progress has been made in the diagnosis of diseases of the urinary tract in children with the aid of both the examining and catheterizing cystoscope. Instruments for this purpose are now made of the smallest calibre. It is possible to cystoscope a male

child of two years of age without seriously damaging the urethra. As a result many congenital lesions of the prostatic urethra, internal meatus, ureters, and kidneys are diagnosed in early life, whereas a few years ago these were not recognized until complications had occurred.

Before use care should be taken to remove any foreign body from the *Care of* ocular end of the telescope or the window, for owing to high magnifica- *instrument* tion it will obscure the field of vision. To avoid scratching the glass the softest material must be used for this purpose. The metal sheath into which the telescope is inserted has a valve at its proximal end and at its distal end the electric lamp. At the end of a catheterizing cystoscope there is a lever for directing the catheters towards the ureteric orifices. After use any clots, mucus, or thick pus sticking to the interior of the sheath must be forcibly ejected by fixing the proximal end to a cold-water tap with a fine jet. It is equally important to cleanse the valve separately, and for this it should be removed from the sheath. After the whole instrument has been boiled it is necessary to dry it with methylated spirit before returning it to its case, which is constructed so that it can also be boiled. When the cystoscope is next required for use there is no need to remove it from the metal container in order to sterilize it. The case and contents are placed together into the sterilizer.

The source from which the electric current is obtained to light the *Source of* lamp should be a dry-cell battery of about eight volts, with a rheostat *electric* to regulate it. A cystoscope lamp usually requires three and a half volts. *current* If the current is taken from the main electric supply by the aid of a transformer, there is always danger of blowing the lamp. The cable should be so constructed that it can be boiled.

(2)—The Examination

(a) Position of Patient

The patient may be placed in one of two positions for cystoscopy, namely on his back with a cushion or sandbag beneath the buttocks to elevate the pelvis, or in the lithotomy position. The latter is more convenient for examination of the female bladder and in both sexes for catheterization of the ureters.

(b) Choice of Anaesthetic

An anaesthetic is not needed for cystoscopy in the female, for the urethra is short and easily dilated. In the male a local anaesthetic similar to that used for urethroscopy should always be given (see p. 24). If the patient is very sensitive to pain it may be necessary to submit him to a low spinal or general anaesthetic. Gas and oxygen are all that *Low spinal* is necessary for the latter, and for the former the technique in use at *anaesthesia* St. Peter's Hospital, London, may be adopted. The patient is placed in a sitting position and, with strict aseptic precaution, 0·4 c.c. of a 10 per cent solution of amylocaine hydrochloride (stovaine) in glucose is injected by means of a syringe and needle into the spinal canal between the third and fourth lumbar vertebrae. After an interval of two minutes

he lies down. By this method the whole of the urethra and the internal
meatus are anaesthetized, bladder sensation remaining intact. Sacral
anaesthesia is also sometimes employed, but it has no special advantages.
As soon as the urethra has been rendered insensitive by one of the
methods described, the patient is placed in position for the cystoscopy
and the external meatus swabbed with a weak antiseptic.

(3)—Technique

Immediately before using the cystoscope the urologist must be satisfied
that the electrical equipment and above all the lamp are working
efficiently. Re-insertion of the cystoscope because the lamp has fused
at the commencement of the examination of the interior of the bladder
will increase the trauma to the urethra and reduce the confidence of the
patient in his surgeon.

*Insertion of
instrument*
The insertion of the cystoscope into the female urethra does not require
any special skill or training for the same reasons that anaesthesia in this
sex is unnecessary. On the other hand a delicate sense of touch, only
acquired by experience, is needed to pass this instrument into the male
bladder without causing damage to the urethral mucous membrane.
The curves of the male urethra are straightened out during the passage
of the cystoscope and it follows that, if force is used or the instrument
pushed in the wrong direction, much trauma will be done.

Lubricants
The introduction is made easier by lubricating the whole of the shaft
of the cystoscope rather than just the beak. The best lubricant is sterile
liquid paraffin, though for convenience various antiseptic jellies put
up in metal tubes may be used. Glycerin is sometimes recommended,
but it irritates the mucous membrane, and any chemical substance which
acts thus must be avoided.

*Insertion of
instrument*
In the male the cystoscope is inserted by passing it along the anterior
urethra as far as the membranous portion with the penis on the stretch
and at right angles to the pubes. The instrument is then gently depressed
between the thighs and carefully guided through the prostatic urethra.
It is at this point that the beak of the cystoscope may be held up and
will require skilful manipulation to coax it over the verumontanum and
through the internal sphincter. In such circumstances if force is used
there is danger of making false passages in the prostate.

It is on record that the beak has been driven through the urethra into
the rectum. As the lining membrane of the urethra is not under direct
vision it is constantly treated with scant respect, and yet it is just as
delicate as the conjunctiva. Unseen tissues are not necessarily insensitive.
Both the undergraduate and the postgraduate student must be taught
to insert instruments into the urethra with the greatest gentleness.
Haemorrhage, however slight, shows that a false passage has been
made.

Irrigation
As soon as the cystoscope has been inserted into the bladder the
telescope or obturator is removed and the urine is evacuated. The
cystoscopist then proceeds to irrigate the bladder until satisfied that the

medium through which he will make his observations is clear. A weak antiseptic should be used for this purpose at a temperature of 90° F., boric acid lotion, saline solution, and mercuric oxycyanide 1 in 8,000 being the antiseptics commonly used. The mucous membrane of the bladder is much more sensitive to heat and cold than the skin, and therefore a fluid which feels only warm to the latter may cause pain when in contact with the bladder wall. For irrigation either a metal syringe or a glass douche-can with a rubber tubing attachment may be used, the latter being preferable. It is convenient to fix the distal end of the rubber tube to a two-way cannula, which is introduced into the valve of the cystoscope, thus allowing free ingress and egress of the antiseptic lotion.

During the irrigation it is advisable to test the bladder capacity by allowing the fluid to run in until the patient complains of distension. *Test of bladder capacity* The normal content without causing discomfort is about fifteen ounces. Inability to hold less than this amount indicates irritability of the bladder. In the presence of haematuria it may be necessary to use an astringent fluid such as silver nitrate 1 in 5,000 in order temporarily to control the haemorrhage. The slightest tinge of red in the medium interferes with accurate observation. The degree of cloudiness or discoloration of the lotion as it flows out of the cystoscope is tested by allowing it to run into a small glass receptacle such as a medicine measure.

With the most modern cystoscopes there are facilities for continuous irrigation, which is often necessary in cases of persistent haemorrhage during the examination.

The investigations of lesions of the urinary tract by the aid of the cystoscope must be carried out systematically. It is wise at the com- *Routine of complete examination* mencement to make a rapid survey of the whole of the interior of the bladder. Then should follow an examination of the trigone bounded above by the inter-ureteric bar and below by the internal meatus. A careful study of the condition of the latter is the next step, and finally the ureteric orifices must be found and watched for muscular movements and efflux of urine.

(a) Examination of the Bladder

In the preliminary examination of the bladder mucous membrane the following points must be noted. If the bladder is quite healthy it is *Colour* straw-coloured and in the child much paler. The colour in inflammation may be anything between pink and deep red.

The surface is quite smooth in the normal bladder, but when the *Surface* muscular coat is hypertrophied, as happens in the early stages of prostatic obstruction and urethral stricture, bands of muscle-fibres, retiform in arrangement, stand out and produce the condition of trabeculation. When the hypertrophy is followed by atrophy, the bladder wall gives way between these muscle bands and depressions are observed; this is called sacculation. In paralysis of the bladder the trabeculation is made up of much finer interlacing strands. Owing to the inability of the rays

of light from the cystoscope lamp to penetrate to the bottom of a saccule, the cystoscopic appearance is like that of looking into a cave: all is dark within, but the arrangement of the structure which surrounds the exit is clearly visible.

Presence of oedema or new growth

When a localized swelling is observed it is necessary to determine whether it is oedema or new growth. This is not difficult, for in the former condition the swelling fades away into the surrounding mucous membrane, whereas in the latter it is discrete. Should a tumour be diagnosed the cystoscopist must take accurate note of the character of its surface, the presence or absence of a pedicle, and vascular changes of the mucous membrane around it. Non-malignant growths are pedunculated and have thin finger-like processes spreading out from the main stem. The mucosa in the neighbourhood is normal, but in cancer there may be oedema and increased vascularity.

Observation of blood-vessels

The importance of observing the blood-vessels cannot be over-estimated. Just as in retinoscopy it is possible to detect atheroma and arteriosclerosis, so by the examination of the bladder with the cystoscope the diagnosis of a cardiovascular lesion is possible. In this disease the arteries of the vesical mucosa stand out prominently, and the rupture of one or more of them is demonstrated by submucous haemorrhages (see Plate II, D). Increased vascularity of the whole or part of the bladder indicates inflammation.

(b) Of Trigone

The chief characteristic of the trigone, the part of the bladder between the inter-ureteric bar and the internal meatus, is its vascularity, which gives it a pink colour cystoscopically. The inter-ureteric bar is easily distinguishable as a ridge extending across the bladder and separating the straw-coloured mucous membrane of the postero-superior wall from the vascular trigone.

(c) Of Internal Meatus

Normal

The internal meatus as seen by the cystoscopist consists of an anterior lip which when normal appears as a transverse ridge and a posterior lip which merges with the trigone. As most causes of prostatic obstruction alter the shape of the internal meatus, the inexperienced cystoscopist must make himself thoroughly acquainted with its normal appearance.

Abnormal

In adenomatous disease of the prostate one of the earliest cystoscopic signs is an upside-down 'V' shape of the anterior lip. When the disease is advanced, the posterior lip becomes a bulge and sometimes is so large as to obscure the view of the trigone. It is erroneously called the middle lobe of the prostate.

(d) Of Ureteric Orifices

The ureteric orifices are situated on either side of the inter-ureteric bar and normally appear as tiny slits. There is very seldom any difficulty in finding them with a cystoscope. The procedure is to turn the cystoscope

round until the window of the telescope is pointing downwards. The inter-ureteric bar is then located by determining the line of division between the muscular trigone and the comparatively non-vascular postero-superior wall. While the inter-ureteric bar is kept in the field of vision, the telescope is turned half a circle to the left or right, when the orifices will appear at the end of the ridge.

The cystoscopist must then watch very closely for the movements of the lower end of the ureter. It has been mistakenly supposed that there is a sphincter at the ureteral orifice. Actually the movement is telescopic, a muscular wave along the intramural portion of the ureter being clearly visible. If it is very vigorous a foreign body such as a stone may be present, the violent action indicating an attempt at its extrusion. On the other hand complete absence of movements points to a diagnosis of paralysis, chronic ureteritis, or non-functioning kidney. *Movements of ureter*

While the cystoscopist is observing these activities of the lower end of the ureter, he should at the same time watch the character and colour of the urinary efflux. Under normal conditions the urine escapes into the bladder about once a minute, but the rate of flow is affected so readily by emotion and instrumental interference that little heed need be taken of slight alterations in the number of effluxes in a given time. *Urinary efflux*

The expulsive power of the ureter is often an aid to the determination of changes in the wall of the duct. If the ureter is paralysed or much dilated the urine only trickles out into the bladder, and the same effect is produced by tuberculous disease. Again it is important to observe the size of the efflux, for a stricture at the ureteric orifice will cause the urine to be expelled in a thin jet.

Finally the colour and consistence of the urine must be carefully noted. If normal it is crystal clear at the moment of ejection into the bladder. A small quantity of pus or bacteria causes the efflux to appear slightly cloudy, and in haematuria smoky or bright red according to the amount of blood. Sometimes when severe bleeding is beginning to subside, the urine on expulsion is of the same colour and consistence as treacle. Pyuria too if severe will produce an efflux that has the appearance of thick cream. A milky urine is due to phosphaturia, a large amount of thin pus, or chyluria. *Character of urine*

(4)—Use of Cystoscope in Treatment

Many ingenious instruments apart from catheters and bougies have recently been devised which can be passed through a cystoscope for the treatment of lesions of the bladder, prostate, and the lower ends of the ureters.

A cystoscopic lithotrite has been introduced which permits of stone-crushing under direct vision. A word of warning is necessary with regard to the use of this instrument, for the lithotrite portion is easily broken if an attempt is made to crush a large or hard calculus. Its use should be limited to stones about the size of a cherry and composed of calcium phosphate. *For cystoscopic lithotrity*

For diathermy   The treatment of growths of the bladder, in particular a simple papilloma, has been revolutionized by the introduction of the diathermy current. Electrodes of different sizes can be passed into the bladder with the aid of the catheterizing cystoscope and the tumour fulgurated. The electrode is guided to the area which requires treatment by the lever at the end of the cystoscope.

For growths situated around the internal meatus and the anterior wall, it is necessary to use a cystoscope with a retrograde telescope and a retrograde lever. With this instrument the cystoscopist is enabled to look directly backwards at the internal meatus.

For impacted stone   Various diseases of the lower end of the ureter can be successfully treated by cystoscopic instruments; for instance a stone impacted at the ureteral orifice may be expelled into the bladder by dividing the last quarter of an inch of the wall of the duct with scissors, one of the most ingenious instruments which can be passed through a cystoscope. The same operation may be performed with the endothermy needle which cuts through the tissues with amazing rapidity (see Plate II, E and F). Again a special dilator may be used for stretching the ureter. This is a cunningly devised instrument. For all these operations a cystoscope of either the Swift Joly or Winsbury White pattern must be used.

For prostatic obstruction   Attempts have recently been made to treat various forms of prostatic obstruction with the assistance of the endothermy current. Again this has only been made possible by knowledge of the appearance of the prostatic urethra and internal meatus acquired with the cystoscope. The instrument is known as the resectoscope and consists of a telescope, an insulated sheath, and a specially constructed endothermy electrode which is either a wire loop or a tube known as a punch. With one or other of these electrodes a considerable amount of tissue in the region of the internal meatus can be removed.

Thus there are many diseases of the internal meatus, the bladder, and the ureteral orifices which can be treated successfully with the aid of the cystoscope, but accurate interpretation of the pathological changes observed with this optical instrument is acquired only by many years' experience.

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ENEMAS AND COLONIC IRRIGATIONS

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Reference may also be made to the following titles:

1.–USES OF ENEMAS

414.] An enema—formerly called a clyster—is a liquid or gaseous substance, either medicinal or alimentary, injected into the rectum. The term colonic irrigation is used for special forms of enema designed to cleanse and soothe the bowel. The use of enemas dates from very early times. Celsus wrote: 'There should be introduced into the bowel simply water when we are content with a gentle remedy, or hydromel as one a little stronger; or as a soothing enema a decoction of fœnugreek, or of pearl barley, or of mallow (or as an astringent clyster a decoction of vervains), but a drastic one is sea-water or ordinary water with salt added; the better in both instances for boiling. A clyster is made more drastic by the addition of olive oil, or soda, or honey: the more drastic the clyster, the more it extracts, but the less easily it is borne. The fluid injected should be neither cold nor hot, lest either way it should do harm. Following upon the injection the patient ought to keep in bed as long as he can, and not give way to his first desire to defaecate;

then go to stool only when he must. In this way generally when the material is extracted, and the upper parts relieved, the disease itself is mollified.' Celsus also mentioned the introduction into the bowel from below of barley or gruel, to support the patient's strength in conditions of collapse. John of Arderne (1306‑90), who first practised in Newark and later in London, used irrigation of the bowel for intestinal colic.

Uses of enemas

The present-day use of enemas has the objects of (1) stimulating peristalsis in order to evacuate faeces and gas from the bowel, (2) clearing the intestinal lumen of mucus and bacteria, (3) applying various astringent and healing medicaments, (4) furnishing the patient with additional water and nourishment, (5) giving drugs and anaesthetics per rectum, and (6) filling the colon with material opaque to X-rays for diagnostic or therapeutic purposes.

2.—CLEARING ENEMAS

Technique

Before using an enema for the relief of constipation and distension, it is wise to examine the rectum digitally so as to exclude the presence of a ball of retained faeces which cannot be expelled because of poor muscular power or because an inflamed pile or fissure causes spasm of the rectal sphincter. Local treatment is needed for the latter, and in the former case the mass must be broken into smaller pieces by the forefinger covered with a glove and well lubricated with olive oil or liquid or soft paraffin. A wooden or metal spatula or the handle of a spoon may be used. The patient should lie on the left side in a comfortable posture, rather across the bed so that the buttocks come well to the side of the bed. He should be covered with blankets and towels for warmth, but there should be good exposure of the anal orifice and the enema should be introduced under the guidance of the eye rather than by touch. In patients after operation, or cardiac patients who cannot lie down, the enema may be introduced with the patient in the dorsal position, while sitting on the bed-pan. This can be carried out by a skilled nurse, but the left lateral position is better and when possible should be used. The enema and apparatus should be prepared before arranging the patient. The two usual methods are by tube and funnel and by Higginson's syringe. The tube is a soft rubber catheter with round end and eye at the side, size Jacques' 14, attached to a glass funnel by a length of rubber tubing ($1\frac{1}{2}$ to 2 feet) and a glass connecting tube. The end of the catheter is lubricated with liquid or soft paraffin, compound tragacanth paste B.P.C., or K.Y. jelly, and the tube and funnel filled with the solution to be used, to drive out all air. Glycerin as a lubricant is irritating. If an operation on the rectum is to follow, soft paraffin should not be used, but a water-soluble lubricant, such as compound tragacanth paste. The tip of the catheter is passed through the anus and introduced about three inches. The patient is instructed to continue breathing steadily and not to strain. Two persons

may be needed, one to hold the funnel and clamp the tube, the other
to introduce the catheter; but a skilled nurse can hold the funnel and
tube in the left hand and pass the catheter in with the right without spill-
ing. The funnel is raised to about two feet above the bed and the fluid
run in slowly, the patient meantime taking a series of deeper breaths.
About 1 to 1½ pints of fluid are given. In using the Higginson's syringe
three points must be attended to: the syringe must be emptied of air by
pumping several times with both ends of the syringe submerged in the
fluid used; the nozzle should have a rubber catheter which alone is
passed into the rectum; and the pumping should be done with a series
of steady half-strokes to produce a stream with waves rather than a jerky
injection which causes discomfort and may make the patient want to
evacuate the bowel before the full amount is given. The nurse must be
prepared to slow the injection or to stop for a moment or two if the
patient has an urgent desire to evacuate during its administration.

In mild cases of constipation the clearing enema may consist of tap *Solutions*
water only, warmed to body temperature. Injury may be caused by *used for*
enemas that are too hot. In order to stimulate peristalsis further, a weak *constipation*
solution of green soft soap is used, obtained by beating up a heaped
teaspoonful in a quart of warm water. Soap should not be used
repeatedly, as it tends to irritate the rectal mucous membrane. It may
be made less irritating by adding olive oil; two or three tablespoonfuls
of olive oil are emulsified with a little soapy water by beating with the
hand in a bowl and the rest of the soapy solution is added. A more
stimulating enema is one teaspoonful to one tablespoonful of turpen-
tine. The teaspoonful is the usual dose, but larger doses may be used.
This is first emulsified in a little soapy water or in starch paste and dil-
uted by stirring in the remainder. Much relief is thus obtained by stimu-
lating peristalsis of the bowel and expelling retained gases. One or two
teaspoonfuls of glycerin injected into the bowel with a small (2-drachm)
syringe having a slightly curved vulcanite nozzle may be used carefully
by patients or by nurses in cases of habitual retention of faeces in the
lower sigmoid and rectum in adults and children, to form a habit of
better evacuation. A glycerin suppository is more convenient and safer.
In severe cases of constipation, 3 or 4 fluid ounces of warm liquid paraffin
or olive oil with 2 or 3 drachms of turpentine may be first run in, to
soften the retained faeces, and half to one hour later an enema given.
Enemas of sulphates are little absorbed and by hygroscopic action
dilute the bowel contents. A solution of sodium sulphate (3 to 5 per
cent in water) is useful for repeated enemas, as it stimulates bowel
contraction. Magnesium sulphate on the other hand relaxes the bowel,
and a 10 per cent solution relieves post-operative spasm. Probably the
most efficacious evacuating effect is obtained by using the natural action
of bile. The ox-bile enema consists of 1 ounce of purified ox bile dis-
solved in very hot soapy water. The ox bile is very thick and should be
mixed first with a little hot fluid and then made up to one pint. As soon
as it becomes cool enough to be given safely, the whole pint is injected.

Less than 1 ounce of the purified ox bile is useless. It may be conveniently kept in ointment-pots each containing 1 ounce. It may be used with success when ordinary enemas are ineffective in very constipated patients or those with obstruction; also after operation if the ordinary aperient is not quickly effective or is vomited. Relief may be obtained from distension and wind evacuated from the otherwise empty bowel after operation by injecting a solution of sodium chloride, 15 grams, in water 100 c.c. at 100° to 104° F. This acts by increasing intestinal peristalsis; it is useful in peritonitis. A carminative effect is produced by an enema containing peppermint water, which may be used after a flatus tube has relieved wind in the lower bowel.

Precautions   Irritation of the rectal mucous membrane by repeated enemas of soap has already been mentioned. Over-distension must be avoided. A rubber catheter should be placed over the nozzle of Higginson's syringe to prevent rectal injury. Such injuries are not rare and may occur without gross carelessness from poor exposure, bad lighting, insufficient lubrication, the use of force, or the presence of rectal conditions such as prolapsed haemorrhoids. The mucous membrane of the rectum is not very sensitive and may be ruptured without severe pain, but the injection of soap into the submucous tissues causes agonizing pain. Sloughing of the mucous membrane may take place with subsequent contraction which may necessitate colostomy, and death from peritonitis has resulted. The enema habit in neurotic patients requires sympathetic explanation to the patient with re-education in the proper method of evacuating the bowels.

Enema rashes and dermatitis   Enema rashes are occasional complications and may be troublesome. In the mildest forms there is a blush beginning on the buttocks and around the middle. The patient complains of pricking at first, and the rash is irritable and burning rather than itchy. It may be papular at first, and become confluent, or may begin as a bright or dull red erythema. The usual site is on the buttocks and abdomen, and it may spread to the thighs and legs, and occasionally the arms. In one case the feet and hands were first affected, then the limbs and face, but not the trunk. In another case the parts first affected were the buttocks and backs of elbows, but later the rash became general. In a few cases there has been a widespread dermatitis with high fever, delirium, and much constitutional disturbance, followed by branny scaling. In another group of cases there seems to be a stirring up of anal eczema which spreads to the genitals and sometimes to the rest of the body. This form is accompanied by severe itching. In one severe case of this nature, water only had been used for routine enemas on alternate days in a patient confined to bed. In some instances the soap used for the enema has been held responsible, and potassium ('soft') soaps are recommended in preference to soda soaps. In others it is believed that intestinal toxins are the cause, and that these are more readily absorbed when the enema or colon irrigation is not evacuated. That an allergic reaction may be responsible is suggested by the fact that one patient remembered having had a

similar rash after enemas many years before. In such cases it may be *Treatment* best to omit treatment by enemas or irrigations; but these may sometimes *of enema* *rashes* be resumed later without recurrence. In simple cases a dusting powder containing equal parts of zinc oxide, starch, and boric acid, applied freely, gives relief; or a lotion containing one drachm each of zinc oxide, calamine, and glycerin, 10 minims of solution of coal tar, and water to one fluid ounce, to which mercuric chloride may be added in the proportion of 1 to 3,000. In the eczematous group, liniment of calamine is useful. In severe cases of dermatitis, a milk diet of two quarts in twenty-four hours may be enjoined; three parts of milk (hot or cold) with one part of soda water may be given in quantities of 6 fluid ounces every two hours. The bowel should be cleared with repeated $\frac{1}{4}$-grain doses of calomel, which may be followed by castor oil, and then a mixture containing:

Salol	–	–	–	–	– 5 grains
Sodium bicarbonate	--	–	–		– 15 grains
Bismuth carbonate	--	--	–		– 30 grains
Chloroform water	--	--	–		to 1 fl. ounce

Dose: Two tablespoonfuls three or four times a day.

Relief for the skin is more satisfactorily obtained by a bath containing 20 grains of potassium permanganate in 30 gallons of water, or by dabbing the affected skin with a lotion containing 0·1 grain of potassium permanganate to one fluid ounce of water. After drying, the following ointment is applied:

Bismuth carbonate	–	–	–	– 120 grains
Rose water ointment	–	–	–	– 120 grains
Yellow mercuric oxide ointment		–		– 240 grains
Zinc oxide ointment	–	–	–	– to 2 ounces

In my experience ichthammol in glycerin has not been successful.

3.—CLEANSING ENEMAS (COLONIC IRRIGATIONS, INTESTINAL DOUCHES)

Cleansing enemas are used to wash from the bowel abnormal mucus, toxic products, and bacteria. Experience with barium sulphate enemas given under observation on the X-ray table shows that the liquid, passed so gently into the colon that it does not excite defaecation reflexes, reaches the caecum and terminal part of the ileum. The method recommended is with a single tube, but many others have been used; of these the most usual is a modification of the double-tube, with separate inflow and outflow.

An ordinary colonic irrigation is given with the patient on a couch or *Technique* bed, lying on the left side with knees drawn up. The solution having been prepared—usually physiological or slightly hypotonic salt solution (0·6 to 0·8 per cent)—is placed in a reservoir at a temperature of 104°

to 106° F. The reservoir is arranged so that the top of the fluid is about two feet above the couch. The tube and catheter (size 12 to 16) are first *Introduction* filled with fluid and the tap is turned off. The catheter lubricated with *of catheter* soft paraffin or jelly is introduced about four inches into the rectum. This should be done with a clear view of the anus, and the patient should be instructed to make a slight bearing down or expulsive effort while the tube is being introduced. It then slips in without discomfort, even when there are tags of mucous membrane or small piles. The tap is then turned on and the patient is told to breathe more deeply than usual. From 20 to 30 fluid ounces are run in gently in seven to ten minutes. If discomfort or sense of fullness occurs, the flow is regulated by the tap and the patient is told to take deep breaths, thus relaxing the muscles of the abdominal wall. After the injection of more than a pint, the catheter is gently withdrawn without spilling any fluid, and the patient turns onto the back, or better onto the hands and knees, for three minutes taking several deep breaths, then onto the right side for three to five minutes with deep breathing. This injection is then evacuated. It serves to clear the bowel. A second injection is then made in the same way and cleans the bowel. In capable hands the whole procedure runs smoothly, the patient is comfortable during the injections, is relieved by the evacuation, and is free from reaction afterwards. Discomfort may arise from insufficient lubrication of the catheter, forcible introduction, inflamed piles or fissure, and pressing the tube in too far. X-rays show that when attempts are made to introduce the catheter more than six or eight inches it usually fails to pass the recto-sigmoid angle and coils up in the rectum. In straining babies with acute enterocolitis it may be possible to introduce the tube further, so that the contents of the descending colon are siphoned out readily. In conditions of spastic colon the patient may find difficulty in returning the fluid injected, or it may be retained for a time and then passed in gushes during the next few hours. The fluid thus returned may be faecal from rapid passage through the bowel of matter from the lower ileum. Patients likely to be perturbed by these happenings should be reassured, and after a course of douches normal return of the fluid injected is usually obtained. Some complain of undue abdominal distension if the fluid is injected too rapidly or under too great pressure. A careful operator can carry out the treatment, even in a highly nervous patient, by taking proper precautions and giving quiet and confident reassurance.

Reactions of Some untoward reactions may, however, occur: in patients with spastic *patient* colon, nausea or epigastric pressure may be felt, sometimes cramps, and, after the irrigation, a sense of weakness. Anal irritation may follow the passage of acrid matter from the bowel; bleeding may occur, usually from haemorrhoids, sometimes from a fissure, ulcer, or torn polypus. Perforation of the sigmoid from distension has been reported.

Method using Many workers prefer to use two tubes, a separate inflow and outflow. *two tubes* These may be of 24 and 30 calibre, the outflow being the larger. A large volume (6 to 10 gallons or more) is run through; usually water is used,

again under low pressure. There are numerous modifications in which the patient sits in a bath with the two rectal tubes inserted and a continuous flow of fluid maintained; there is no evidence that, once the proximal colon is filled, the fluid does more than circulate round the ends of the tubes.

Intestinal irrigations are given two or three times a week at first, and later every five or seven days. It is usually noted that at first much faecal debris and some mucus are evacuated, and a reflex secretion of excessive mucus may be caused in those who passed none before, which ceases when the gut is more used to the injection. This has been sometimes wrongly explained by bath attendants as a washing out of accumulated slime which is later no longer formed. In severe colitis, however, the amount of mucus often diminishes as the bowel is soothed by treatment. Too much irrigation may excite the production of mucus, just as overdosing with aperients does, and may wash away much absorbable nutritive matter from the bowel. There is also the risk that in neurotic subjects an irrigation habit may be formed.

The customary wash-out consists of water or hypotonic saline. Physio- *Solutions* logical salt solution may give rise to thirst or activate the bladder. Weak *used* solutions (1 per cent) of sodium bicarbonate are used to dissolve mucus, but may cause griping and frequent urination. The object is to wash the bowel, and the strongest permissible antiseptics have very little effect on the bacteria present. The intestinal antiseptic selected must be little if at all absorbed or it may exert a systemic action; it must not cause any local irritation of the bowel wall and must still possess antiseptic properties when mixed with the intestinal contents. The direct application of antiseptic solutions does not destroy all bacteria or inhibit the production of intestinal poisons. Of the permissible antiseptics, those *Antiseptics* in use are acriflavine 1 in 8,000, mercurochrome 1 per cent, monsol 1 in 500, chinosol 1 in 20,000, and potassium permanganate 1 in 10,000. As astringents in ulcerative colitis, albargin 1 grain to 1 fluid ounce of *For ulcerative* saline, mild silver proteinate (argyrol) 0·5 per cent solution, silver pro- *colitis* teinate (protargol) 1 per cent, collargol 3 per cent, tannic acid 60 grains to 1 pint, and alum 0·5 per cent are used. Silver nitrate should be given with care, beginning with low strengths, e.g. in a sensitive bowel, 0·01 per cent, but usually 0·1 per cent, rising gradually up to 0·4 per cent. In amoebic dysentery, emetine hydrochloride (2 grains to 1 pint), acet- *For* arsol (stovarsol) 1 per cent, or chiniofon (yatren) 0·5 to 2 per cent has *dysentery* a specific action, and for ciliate dysentery, methylene blue 2 grains to 1 pint. Threadworms are treated with enemas of quassia infusion, or *Thread-* hypertonic salt solution (two or three teaspoonfuls to one pint). Sooth- *worms* ing enemas contain bismuth carbonate or oxychloride (10 to 20 grains *Soothing* *enemas* to 1 fluid ounce of water). An emulsion of the bismuth salt in liquid paraffin run in warm and retained is more comfortable. Lead acetate 1 per cent, or 1 drachm of 1 in 1,000 adrenaline in ½ to 1 ounce of water, may be used for bleeding from piles. Ice-water enemas have *Piles* been used for reducing temperature in hyperpyrexia. *Hyperpyrexia*

4.—MEDICATED ENEMAS

The most useful of all medicated enemas is that of starch and opium (30 drops of tincture of opium in 1 ounce of thin starch mucilage). Digitalis, salicylates, bromides, and chloral hydrate can be administered per rectum in unconscious or very ill patients. Rectal anaesthesia is dealt with in another section (see ANAESTHESIA, Vol. I, p. 496; and for rectal anaesthesia in children, CONVULSIONS IN INFANCY AND CHILD-HOOD, Vol. III, p. 411).

5.—OPAQUE ENEMAS

Enemas of barium sulphate or of bismuth carbonate or oxychloride emulsions are used for X-ray diagnosis and have been tried in the reduction by manipulation of intestinal intussusception (see also article RADIOLOGY IN DIAGNOSIS AND TREATMENT).

6.—NUTRIENT ENEMAS

The principal absorptive function of the colon is concerned with water. Some of the carbohydrates (dextrin and dextrose) and albumose-peptone mixtures are absorbed, but the fats and natural proteins scarcely at all. The claims made for the treatment by rectal feeding of peptic ulcers and other chronic disorders have not been substantiated, since not enough nourishment can be absorbed in this way in twenty-four hours to give a sufficient caloric intake. Partly digested meat and milk and various pancreatized proteins are absorbed little, if at all, and are retained with difficulty and voided quickly because irritating.

Water or weak saline may be absorbed in considerable quantities from the bowel, and alcohol up to 3 per cent by weight can be retained and absorbed. The foodstuffs given should be as far as possible isotonic, the peptone and dextrin recommended being in salt solution. Von Noorden used the following: Witte peptone 30 grams, dextrin 50 grams, alcohol 9 grams, sodium chloride 2 grams, water 300 grams, with 5 to 7 drops of tincture of opium. To be retained each enema should not be more than 300 to 400 c.c., and this can only be repeated two or three times a day. Thus not more than 1,200 calories can be given in a day; not more than about half the basal needs of the body can be retained in the rectum, and it would be unlikely for all of this to be absorbed. Rectal feeding is thus limited, for full and sufficient feeding per rectum is not possible. 'Of vaunted rectal foods now remain only water and—more as ornamental additions than great energy sparers—the carbohydrates and dilute alcohol' (Boas). An hour before giving von Noorden's enema the bowel should be cleared with an enema of warm physiological

saline or of camomile infusion; the nutrient, which is at body temperature, is given slowly through a soft Nélaton 6 catheter lubricated with olive oil or K.Y. jelly and inserted 3 to 4 inches.

In unconscious patients, or after operation, or if vomiting prevents feeding by the mouth, fluid, usually physiological saline, with or without 5 per cent of glucose, may be given per rectum, either in amounts of 15 to 20 fluid ounces every 4 to 6 hours or by continuous drip. In the former method the fluid is given by tube and funnel as described above. When using the continuous drip method it is important to regulate the flow, to prevent too great a pressure being used, and to keep the fluid when it reaches the bowel at body temperature. This may be carried out by using a thermos flask from which the fluid is siphoned. On the connecting tube from the flask to the rectal catheter it is convenient to have a drip apparatus, so that the rate of flow is regulated. This part of the apparatus must be kept warm by contact with an electric bulb; otherwise the fluid cools too much in the length of tubing required. By this means 4 to 6 pints of fluid may be given and absorbed in the twenty-four hours. Though isotonic solutions are least irritating to the mucous membrane of the bowel, better absorption of fluid and thus better thirst-quenching are obtained by using slightly hypotonic solutions. One recommended contains 1 per cent glucose, 0·4 per cent sodium chloride, and 0·4 per cent sodium bicarbonate. The last seems to promote absorption more than other salts.

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ENOPHTHALMOS AND EXOPHTHALMOS

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1.–ENOPHTHALMOS

Causes 415.] The eye may sink back into the orbit when the orbital contents are diminished as in severe emaciation, within a few hours of the onset of Asiatic cholera, and after removal of an orbital neoplasm. Enophthalmos is a remote complication of some orbital injuries, the globe being drawn back by cicatricial contraction or parts of the orbital rim becoming displaced forwards by an indirect fracture, thus increasing the

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volume of the orbit. Other causes are depressed fractures of the upper jaw and the malar bone, and cellulitis with subsequent fibrosis. Enophthalmos occurs on adduction of the eye in cases of congenital paralysis of the external rectus muscle. It is also evident in lipodystrophia progressiva and in some cases of facial hemiatrophy.

2.–EXOPHTHALMOS

(1)—Definition

416.] Exophthalmos is the term applied to forward displacement of the eye. This abnormality may be caused by an increase in any of the orbital contents, by a loss of tone or paralysis of the extra-ocular muscles, and by congenital anomalies in the development of the osseous wall of the orbit as in oxycephaly. It occurs in leontiasis ossea and in high myopia.

(2)—Causes

For the purpose of convenience the aetiology of exophthalmos is classified as follows:

(a) Congenital

In oxycephaly the orbits are set more widely apart and are shallower than is normal (see OXYCEPHALY). *Oxycephaly*

A meningo-encephalocele is generally situated in the upper and inner angle of the orbit and is attached to the adjacent bone, which may reveal an osseous defect. Other signs of importance are pulsation synchronous with respiration and the pulse, an increase of the swelling on straining, a diminution of its size on pressure, and evacuation of cerebrospinal fluid if an aspiration needle is used for exploratory purposes. In cases in which there is a large hole in the orbital wall it is necessary to effect closure of this by ligaturing the meningeal sac wall across it and reinforcing this with an osteoplastic flap. Meningitis is a post-operative complication in some cases. *Meningo-encephalocele*

A dermoid cyst is situated in the upper and outer angle of the orbit more prevalently than elsewhere. *Dermoid cyst*

Orbital blastocytomas and teratomas are very rare. They are composed of epiblastic tissue, connective tissue, and hyaline cartilage. The eye on the affected side is often maldeveloped. *Tumours*

(b) Injury

Exophthalmos may be caused by injuries which lacerate orbital blood-vessels producing an orbital haemorrhage, and by fractures which effect a communication between the accessory nasal sinuses and the tissues of the orbit leading to surgical emphysema.

Less immediate causes of exophthalmos after trauma are cellulitis of the orbit following a perforating wound with or without retention of a foreign body, the formation of an abscess or granulation tissue around *Complications following injury*

a foreign body, and the production of an arteriovenous aneurysm by a rupture of the internal carotid artery into the cavernous sinus.

(c) Inflammation

Orbital cellulitis, cavernous sinus thrombosis, inflammatory oedema, exudate, pus, and granulation tissue may cause exophthalmos (see Fig. 6). Importance should be attached to a history of a perforating wound of the orbit, a fracture, traumatic periostitis, nasal sinusitis, dental sepsis, pyaemia, facial erysipelas, meningitis, the acute exanthemata, tuberculosis, syphilis, and actinomycosis.

Symptoms

The symptoms and signs are generally sudden in onset, of rapid progress, and accompanied by a raised temperature and pulse and leucocytosis in the acute stages. The position into which the eye is displaced may afford some clue to the origin of the infection. In frontal sinusitis with orbital extension the eyeball is displaced downwards and outwards; in anterior ethmoiditis, which is more common in children, the displacement is to the temporal side; when the antrum is involved the eye is forced upwards and outwards; and in posterior ethmoiditis with pus or granulations in the muscle cone the eye is pushed directly forwards.

Position of eye

FIG. 6.—Granuloma of orbit. Granuloma inside muscle cone and surrounding optic nerve

In traumatic periostitis the point of maximum tenderness is often along the upper orbital margin, and osteomyelitis may affect the roof, floor, and medial wall of the orbit more frequently than the lateral wall.

Appropriate investigations should be made to ascertain whether the exophthalmos is due to a gumma, a tuberculoma, or actinomycosis.

Treatment

Treatment should be directed towards the cause. In many cases it is necessary to drain an infected nasal sinus by surgical intervention, but in a few conservative measures are sufficient. Syphilis, tuberculosis, and actinomycosis should receive suitable treatment. An intra-orbital foreign body must be removed if active inflammation continues and it is accessible without the risk of inflicting damage to the eye and optic nerve.

Local treatment

The local treatment consists in the application of heat to the orbit, an electric heater or medical diathermy being preferable to hot fomenta-

tions. When an abscess is palpable or localized the orbit should be opened and the pus evacuated. The site of election for an exploratory incision is through the upper lid lateral to the pulley of the superior oblique. In severe cases of exophthalmos in which the cornea is dangerously exposed a tarsorrhaphy is essential to save it from drying and extensive ulceration. Rest in bed, mercurous chloride (calomel), and salines are also of importance.

Panophthalmitis from infective thrombosis of orbital veins, hypopyon *Complications* ulcer, meningitis, and thrombosis of the cavernous sinus are among the more serious immediate complications. Fibrosis with contracture of the internal rectus muscle causing a convergent squint is a remote complication of inflammation in the postero-medial part of the orbit in connexion with the posterior ethmoidal air-cells. Lymphatic obstruction leading to permanent exophthalmos is rare.

Exophthalmos is at first unilateral in cavernous sinus thrombosis and *Differential* in the late stages bilateral in most cases; its onset is late in cases of otitic *diagnosis* origin. Severe supra-orbital pain, abducens palsy, and oedema over the mastoid process at the site of the mastoid emissary vein are clinical features of diagnostic importance. The retinal veins are sometimes fuller than normal and optic neuritis is evident in some cases. The cerebral type of papilloedema is commonest in the otitic cases and when meningitis and a cerebral abscess are present. It is bilateral sometimes but more pronounced on the side of the aural lesion.

The temperature chart is that associated with sepsis; rigors, vomiting, and severe cerebral symptoms also occur. The mortality is very high, but sometimes patients with simple non-infective cavernous sinus thrombosis survive.

In inflammation of Tenon's capsule the exophthalmos is directed *Tenonitis* straight forwards, and all eye movements are limited and painful. The inflammatory fluid may be serous and the condition accompany influenza, gout, or rheumatism. Pus in Tenon's capsule may lead to severe iridocyclitis and panophthalmitis. Treatment is applied to the general physical condition, and locally an electric heater is employed, atropine drops are instilled, and an incision is made if pus points.

(d) New Growths

A number of orbital neoplasms both benign and malignant may cause exophthalmos. Osteomas of the compact type more commonly arise *Osteomas* from the frontal bone, but may be found in the medial wall of the orbit. The cancellous type also occurs. Surgical removal is sometimes very difficult on account of the density of the neoplasm, and it may be necessary to do this operation in two stages. In some cases it is impossible to remove the whole neoplasm on account of its extensive character.

Haemangiomas of the cavernous type may be diffuse or encapsuled, *Haem-* compressible or incompressible. Calcareous deposits in the walls of the *angiomas* cavernous spaces in long-standing cases may afford useful radiographic diagnostic evidence. The encapsulated variety and those which show

loss of compressibility should be excised, and the diffuse, compressible type treated by electrolysis.

Neuro-fibromatosis   Von Recklinghausen's disease (neurofibromatosis) may cause exophthalmos by involvement of either the branches of the fifth cranial nerve in the orbit or the optic nerve. In the former case the skin of the upper lid is hypertrophied and sometimes pigmented; ptosis, forward and downward displacement of the globe, absorption of the orbital walls, and direct transmission of a pulsatile thrill from the intracranial contents are among the commoner physical signs.

Rarer benign tumours   Dermoids, fibromas of the dural sheath of the optic nerve and of the periosteum, adamantinomas, and chondro-myxomas are among the rarer benign neoplasms of the orbit which may cause exophthalmos.

Meningioma

Meningioma of the arachnoid of the optic nerve sheath grows slowly, does not give rise to metastases, but eventually causes death by intracranial extension; it is probably of a very low grade of malignancy. The neoplasm encircles the optic nerve and for a long time compresses it but does not infiltrate it until an advanced stage is reached (see Fig. 7). Fullness of the branches of the central retinal vein, papilloedema, and optic atrophy are physical signs which accompany neoplasms of the optic nerve sheaths.

FIG. 7.—Meningioma of arachnoid of optic nerve. Sagittal section through globe and optic nerve. *a*, Endothelioma in arachnoid; *b*, compressed optic nerve; *c*, fluid beneath detached retina

Malignant neoplasms   Sarcoma of the orbital tissues and the wall of the orbit is commoner in young males 5 to 15 years of age than at other periods of life. The neoplasm grows very rapidly and is highly malignant. Recurrences are common if local removal is attempted, and the sarcoma is in many cases very resistant to deep X-rays and radium.

Carcinoma of the lacrimal gland is primary in origin and of the glandular type. Metastases may occur in the posterior part of the orbit and in the optic nerve.

Extra-ocular extension of sarcoma of the choroid and glioma retinae, glioma of the optic nerve, and fibrosarcoma of its dural sheath may cause exophthalmos. Exenteration of the orbit is necessary in most cases.

(e) *Diseases of the Blood-Forming Organs*

Pseudo-neoplasms causing unilateral or bilateral exophthalmos are present in the orbital tissues in some diseases of the blood-forming

organs, such as leukaemia, chloroma, and lymphocytoma. (See also Vol. I, p. 252.)

(ƒ) Cysts

For dermoid cysts see Vol. III, p. 635. Implantation cysts following a perforating wound and parasitic cysts such as hydatid and cysticercus cysts are rare.

(g) Arteriovenous Aneurysms and other Vascular Changes

An arteriovenous aneurysm between the internal carotid and the cavernous sinus may be caused by trauma, syphilis, or arteriosclerosis and give rise to pulsating exophthalmos. The vessels of the lid and conjunctiva are widely dilated; the angular vein is very full and has a pulse synchronous with that in the carotid artery. The patient complains of a 'rumbling noise like a waterfall' in his head. The degree of exophthalmos diminishes on pressure over the common carotid artery on the same or the other side. The retinal veins are distended, and papillitis and orbital pain, from stretching of the ophthalmic division of the fifth cranial nerve, are present. The exophthalmos rarely undergoes spontaneous subsidence; generally it increases and an intracranial haemorrhage ends the scene.

Intermittent exophthalmos may be provoked in some persons by depressing the head. The jugular vein is compressed and if the orbital veins are in a varicose state they retain an abnormal amount of blood. *Compression of jugular*

In neoplasms of the pituitary gland some degree of exophthalmos is present in a number of cases on account of obstruction to the flow of venous blood in the cavernous sinus. *Obstruction by neoplasms*

(h) Toxic Goitre

For exophthalmos in toxic goitre and following the administration of thyroid extract and thyroxine, see GOITRE AND OTHER DISEASES OF THE THYROID GLAND.

(i) Chronic Nephritis

When uraemia is imminent orbital oedema gives rise to exophthalmos, retro-ocular pain, and limitation of the movements of the eye.

(j) High Axial Myopia

In the high degrees of myopia the antero-posterior length of the globe is considerably increased and there is some forward displacement and apparent exophthalmos.

(k) Obesity

Obesity is responsible for exophthalmos in those cases in which the orbital fat is considerably increased.

(3)—Diagnosis

The investigation of a case of exophthalmos should be directed to eliciting a careful history of the nature of its onset, whether sudden or *Investigation of patient*

gradual, its progress and duration, and its relation to trauma, focal sepsis (particularly in the accessory nasal sinuses adjacent to the orbit), and to any relevant constitutional disorder such as toxic goitre, some anaemias, chronic nephritis, syphilis, tuberculosis, and obesity. The possibility of a metastatic growth should be borne in mind, for a patient is not likely to associate a prominent eye with, for example, the removal of a breast some years previously.

Examination of eye   The position into which the eye is displaced is of considerable diagnostic importance in many cases. By palpation of the orbit the fluid or solid consistence of a newly-formed mass may be detected; its compressibility, changes in volume, pulsatile character, and associated osseous defects should be noted. By auscultation a bruit is audible in cases of arteriovenous aneurysm. Aspiration of a fluid swelling will afford diagnostic assistance in some cases. Oedema over the mastoid process is an important clinical sign in cases of cavernous sinus thrombosis, whether otitic in origin or not. The visual acuity and fields are also of diagnostic assistance in some cases.

Radiography   Radiographs of the skull may reveal shallow orbits and other defects typical of oxycephaly, leontiasis ossea, an osteoma, calcification in a cavernous haemangioma, enlargement of the optic foramen in neoplasms of the optic nerve, the condition of the pituitary fossa, opacities in the accessory sinuses, periostitis of the orbit, and orbital foreign bodies opaque to X-rays, and, following the injection of thorotrast into the common carotid artery, the outline of an aneurysm in the cavernous sinus is demonstrable. A blood examination including a complete blood count and Wassermann reaction is important, and the urine should be investigated for clinical evidence of chronic nephritis.

Blood and urine examination

Bilateral exophthalmos   Exophthalmos is bilateral in toxic goitre, the later stages of cavernous sinus thrombosis, in certain cases of empyema of the accessory nasal sinuses, in symmetrical orbital neoplasms, and in oxycephaly and leontiasis ossea.

Unilateral exophthalmos   It is unilateral in thrombosis of the orbital veins with or without implication of the cavernous sinus, arteriovenous aneurysm, haemorrhage, emphysema, cellulitis, new growths, and cysts.

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ENTERIC FEVERS

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1.–THE ENTERIC GROUP OF FEVERS

417.] Although the incidence of the enteric group of fevers is declining, no civilized country is free from their assault. Before 1880 typhoid fever was a disease of cities, the incidence varying directly with the density of the population; but since then with the steady improvement in sanitation, especially as regards the provision of a pure water-supply and the efficient disposal of sewage, there has been a shift in the incidence of typhoid fever from large towns to rural communities where sanitary conditions are more primitive.

Causal organisms

The enteric group of fevers includes typhoid fever due to infection with *Bacterium typhosum* (*Bacillus typhosus*), and paratyphoid A, B, and C due to *Bacterium paratyphosum A, B,* and *C* (Hirschfeld's bacillus) respectively. In tropical countries the paratyphoid fevers appear to be more prevalent than typhoid. Paratyphoid A is pre-eminent in India and the Orient. In temperate climates paratyphoid B occurs more frequently than paratyphoid A. Paratyphoid C is met with especially in the Balkans.

Course of the disease

The bacilli enter the body through the alimentary tract. The traditional view, that after passing through the stomach they at once set up inflammatory changes in the lymphoid tissue of the intestines, has been largely discarded. They probably penetrate the intestinal mucosa and are carried by the lymphatics, by way of the mesenteric glands and thoracic duct, to the blood-stream. In this way an early bacteriaemia results, but it is transitory, being rapidly brought to an end by the removal of the bacilli by the reticulo-endothelial cells, especially in the liver and spleen. It would seem that the organisms now travel from the liver capillaries to the bile canaliculi and so reach the gall-bladder and intestine. That they can reach the gall-bladder directly from the blood-stream is clear, since little masses of bacilli may be found in the capillaries of the gall-bladder wall in the experimental animal after ligation of the cystic duct. A secondary invasion of the intestine from the blood-stream largely through the agency of the bile is thus brought about, and it is considered that the changes in Peyer's patches and solitary lymph follicles characteristic of the enteric fevers are thus initiated. This conception is largely based on experiments carried out by Ørskov, Jensen, and Kobayashi in experimental mouse typhoid, after infection by the mouth with *Bacterium typhi-murium* (*aertrycke*), and receives support from the occasional recovery of *B. typhosum* from the blood of persons in the incubation period of the disease.

2.–TYPHOID FEVER

(1)—Definition

418.] Typhoid is an acute specific fever characterized clinically by intestinal disturbance, an enlarged spleen, an eruption of rose papules, and a pyrexia of distinctive type. It is the result of infection by

B. typhosum (Eberth's bacillus). Pathologically it is marked by an early bacteriaemia together with swelling and ulceration of the lymphoid tissue of the small intestine, enlargement of the mesenteric glands and spleen, and evidence of toxic changes in the parenchyma of other organs.

First isolation of organism

The bacillus was first obtained from the spleen and mesenteric glands by Eberth in 1880 and was isolated in pure culture by Gaffky in 1884.

(2)—Aetiology

B. typhosum

B. typhosum is a flagellated Gram-negative bacterium, 3μ in length and 0.5μ in breadth. It differs from *B. coli* in not fermenting lactose and in being more actively motile. It produces acid without gas in dextrose, maltose, and mannitol. It causes an initial acidity in litmus milk and fails to form clot. It neither liquefies gelatin nor forms indole. It is killed within 15 minutes by exposure to a temperature of 60° C. It may retain its infectivity in ice for months and can survive for weeks in sterile water, living longer in pure water than in water containing bacteria and protozoa which tend to destroy it. It resists drying. In surface soil it may resist sunlight for 122 hours, but direct exposure to the sun kills it within 8 hours. To animals it is less pathogenic than *B. paratyphosum*. It has been found alive in oysters and mussels which have been living in water contaminated by sewage. It can survive in salt water also.

Incidence

Typhoid fever is most prevalent in temperate and subtropical zones. An epidemic recrudescence appears to occur every 5 or 7 years. Infants are rarely attacked, but the foetus is occasionally affected. It is most frequent in young adults, there being a progressive fall in incidence after thirty. One attack usually confers immunity; but one instance of

Immunity

three attacks has come under my notice. The supposed racial immunity in tropical countries is probably due to the occurrence of infection in childhood.

Sources of infection

Aggregation of susceptible individuals and defective sanitation are the chief factors responsible for its spread in time of war. In England the majority of cases occur during the autumn and are more frequent after a hot dry summer. Infection is derived directly or indirectly from a human source and takes place by way of the alimentary tract. Contact with faeces and urine of patients is primarily the means by which the disease is propagated. When these are properly disinfected and disposed of, and attention is paid to the disinfection of soiled linen, the risk of infection is reduced to a minimum. Fomites such as enema syringes and bed-pans may be a further source of danger; but direct contagion from the sick to his attendants plays a very small part in the spread of the disease. Drinking-water polluted by sewage is chiefly responsible for widespread epidemics. Contamination of the source of supply by the stools of one patient may be sufficient for an extensive outbreak, or defects in pipes may allow infected material to enter in transit. If such a contaminated supply is used to clean dairy utensils or the churns in which milk is stored, rapid multiplication of the bacilli in the milk takes

place, thus favouring propagation of the disease. Butter, cream, or ices may in this way become a public danger, and the same is true of watercress grown in infected water or vegetables such as celery and lettuce if eaten uncooked. Salads in countries where human ordure is used as manure are a recognized source of danger.

The transmission of bacilli from an infected person is not necessarily *Carriers* limited to the period during which the disease is active. Months or years after recovery he may still harbour the bacillus. Such a person is spoken of as a chronic carrier and, if he is in any way concerned with the preparation or purveyance of food, he may be a constant source of danger to the community. Flies, more especially in hot countries, may act as vectors.

(3)—Morbid Anatomy

The characteristic typhoid lesions are inflammatory and affect the *Intestinal* lymphoid tissue of the small and sometimes of the large intestine, the *lesions* mesenteric glands, and the spleen. Peyer's patches and the solitary glands of the small intestine become hyperaemic and swollen. Those near the ileo-caecal valve appear to be most severely affected. This stage usually reaches its maximum by about the tenth day as pinkish-grey elevations of lymphoid tissue. Superficial necrosis of the inflamed patches follows and extends more deeply till, by the end of the second week, the patch is converted into a slough which often shows bile staining. The sloughs separate by ulceration during the third week with the formation of the typical typhoid ulcer with an undermined edge and smooth base. The ulcers resulting from sloughing of the Peyer's patches are ovoid and are seen on the antimesenteric border of the intestine with their long axes parallel to that of the bowel. Ulcers arising in the solitary follicles are more circular. The number of Peyer's patches involved is very variable; in some cases two or three only show ulceration, in others as many as thirty or forty. During separation of the sloughs gross haemorrhage from an exposed vessel, or perforation of the peritoneal coat, may supervene. In mild cases it is thought that resolution may take place without sloughing of the inflamed lymph follicles. In the ordinary type of case, as the ulcers heal, the undermined edges become adherent to the exposed muscle or peritoneum forming the base of the ulcer, granulations appear on the surface, the epithelial covering is restored, and neither puckering nor constriction follows. The process of healing takes place during the fourth week of the illness. In some cases in which there is great prostration, healing is delayed and the ulcerative process may extend so as to cause haemorrhage or perforation even late in convalescence. When diarrhoea has been a prominent feature, there may be extensive ulceration of the solitary follicles of the large intestine in addition to the lesions in the small intestine. A few weeks after the termination of the disease the affected Peyer's patches present the so-called 'shorn beard' appearance, minute black dots on a greyish background.

Mesenteric glands

The mesenteric glands draining the affected part of the intestine become swollen and hyperaemic. Rarely one or more may suppurate and rupture into the peritoneal cavity and set up peritonitis. Cases have been reported in which death has resulted from progressive wasting some weeks after an attack, and post-mortem examination has revealed wide spread atrophy of the mesenteric glands whereby absorption of food from the intestine has been rendered impossible. Typhoid ulcers are very rare in the stomach and oesophagus; but Vinson collected 26 cases of post-typhoidal stricture of the oesophagus. The spleen is enlarged from hyperaemia and cellular hyperplasia, and sometimes shows areas of necrosis and infarcts. In one case I found spontaneous rupture with fatal haemorrhage into the peritoneal cavity.

Stomach and oesophagus

Signs of systemic infection

The usual signs of a systemic infection are present throughout the body; cloudy swelling is seen in the liver, kidneys, and heart muscle. Pylephlebitis is rare. I have once met with a large solitary hepatic abscess. The gall-bladder may show inflammatory changes, and in rare instances ulceration and perforation may have resulted. Gall stones may occur as a sequel. In one case examined after death, I found a gall-stone in a girl of 21, six weeks after an attack of typhoid. Typhoid ulcers have been reported in the common bile-duct.

Kidney and bladder

Considering the great frequency of bacilluria, pyelitis and cystitis are uncommon. Parenchymatous nephritis has been met with occasionally.

Heart

The heart-muscle may show granular degeneration and fatty change. Endocarditis is exceptional. Acute arteritis is very rare (see ARTERIAL DISEASE AND DEGENERATION, Vol. II, p. 44). Statistical records show that arteriosclerosis and atheroma appear to be more frequent in those who have suffered from typhoid. Thrombosis of the internal saphena and femoral veins is not infrequent in cases fatal late in the disease.

Muscle

When no steps were taken to control pyrexia Zenker's necrosis of muscle was common, but it is now rare. The affected portion of muscle loses its colour and becomes semi-translucent, presenting an appearance not very unlike the muscles of a fish. The muscles most commonly affected are the rectus abdominis and the adductors of the thighs. Haemorrhage into the muscle sometimes occurs, or rupture of the muscular fibres may take place.

Larynx

In some cases ulceration occurs in the larynx, and a deep ulcer may be found on the posterior surface between the attachments of the vocal cords. Perichondritis and necrosis of the arytenoid cartilages are sometimes seen, and oedema of the larynx may be the immediate cause of death. The lungs usually show hypostatic congestion, and a terminal lobular pneumonia may be present. In some cases death results from lobar pneumonia, which may go on to abscess formation or gangrene. Cultures taken from the lung show the presence of pneumococci in the majority of cases, accompanied in some by typhoid bacilli. Streptococci are usually responsible for the terminal broncho-pneumonia. Pleurisy apart from pneumonia is unusual; the effusion may be serous, haemorrhagic, or purulent. It is said to be far more frequent on the left side,

Lungs

the proximity of the spleen, an important habitat of the typhoid bacillus, being invoked as an explanation. Infarction from pulmonary thrombosis is occasionally seen.

Subperiosteal suppuration is not very infrequent. The bones most *Osseous* frequently involved are the tibia, ribs, clavicle, femur, ulna, and *system* humerus. In some cases a pure culture of *B. typhosum* has been obtained from the pus; in others it is associated with other organisms, such as staphylococci, streptococci, or *B. coli*. Osteitis and osteomyelitis may also be met with (see p. 62).

A serous or suppurative effusion sometimes occurs in one of the larger *Joints* joints and spontaneous dislocation may have supervened.

(4)—Clinical Picture

The incubation period is usually about 14 days, but varies from 5 to *Incubation* 23. This period is usually free from symptoms, but diarrhoea is some- *period* times present at the beginning, or vomiting in the case of children, both subsiding after a day or two.

The onset is usually insidious. The initial symptoms of feelings of *Onset* lassitude, frontal headaches, nausea, anorexia, chilliness, pains in the back and legs, and muscular weakness gradually increase till after a few days the patient is compelled to take to bed. Sleep is disturbed by dreams and he passes restless nights. Epistaxis occurs in about one-fourth of all cases and slight bronchial catarrh is very common. The temperature usually rises by regular gradations so that the chart shows a step-ladder effect. There is a rise of two degrees or so every evening with a morning remission of one degree, and this continues for four or five days, the maximum being attained before the end of the first week. By this time a little fullness in the abdomen has become evident, and either diarrhoea or constipation prevails. The pulse is quickened but only to a moderate degree, its frequency being less affected than at the onset of other fevers. Occasionally the onset is more sudden, accompanied by rigors, severe pains in the back and limbs, a temperature of 102° or 103° F., and severe prostration so that the patient goes to bed at once.

By the end of the first week the clinical picture is likely to be charac- *Clinical* teristic. The face presents a languid apathetic aspect; the skin is pale *picture at* save for a circumscribed pink flush on the cheeks. The pupils are some- *end of first* what dilated. The lips are dry, parched, and may show desquamation. *week* The tongue, covered by white fur on the dorsum, is red at the tip and edges. The skin is usually dry, though sweatings sometimes occur. Some cases from the fifth to the seventh day show an erythematous blush, and, as the throat is dry and red, a suspicion of scarlet fever may be entertained. On account of the fever and the bronchial catarrh respirations are a little quickened. The abdomen is slightly distended and there is commonly gurgling on palpation over the caecum. The lower pole of the spleen can sometimes be felt. The pulse is somewhat full but easily compressible, and its rate, about 100, is not increased in propor-

tion to the temperature, which has now reached its maximum of 103 or 104° F., though still showing a morning fall of one degree or so. The blood-pressure is rather low from relaxation of arterial tone. The bowels are generally loose, three or four motions being passed in the 24 hours. Typical typhoid stools are semi-liquid, of a pale yellow ochre colour resembling pea-soup, and alkaline in reaction. They are often less offensive than the diarrhoeal dejecta of other diseases. Some patients are constipated throughout and the motions are solid. The urine is high coloured, concentrated, diminished in quantity, and of high specific gravity. It contains an excess of urea and uric acid, but the chlorides are not diminished to the extent seen in pneumonia. It frequently gives a diazo reaction and in severe cases is often albuminous.

The rash   The characteristic rash usually appears on the seventh day, but it may be as early as the fifth or delayed till the twentieth; it may be absent in children and old people. It consists of slightly elevated circular flattened papules, rose pink in colour (rose spots). They measure 2 to 4 millimetres in diameter and are regular in form and are often described as lenticular. Pressure obliterates them temporarily, their colour being due to localized dilatation of capillaries. Exceptionally, a minute vesicle is seen surmounting a papule (roseola vesiculosa). The eruption is often scanty, only three or four papules being seen on the abdomen, with perhaps one or two on the back and flanks or front of the chest. When the eruption is profuse, the papules are thickly scattered over the trunk and may extend to the limbs and rarely to the face. The spots appear in successive crops, each spot lasting three or four days, and the period of eruption may last from ten to twenty-one days. They usually reappear in a relapse and may even come out during convalescence. In the haemorrhagic type of the disease purpuric spots make their appearance. The old physicians used to attach importance to a mouse-like odour about the patient.

In second week   In the second week of the disease the symptoms become aggravated, though the headache is no longer complained of. Prostration increases, wasting and muscular weakness become apparent, and, when left to himself, the patient lies low on his back in the bed. The lips become cracked, the tongue is drier and, as it becomes denuded of its brown fur, is seen to be red and glazed. Sordes accumulate on the teeth. Abdominal distension increases, tenderness, if present, becomes more definite, and diarrhoea is more pronounced. The stools may become darker from admixture of blood. The spleen is larger. Bronchial catarrh increases, and hypostatic congestion of the base of the lungs is usually manifest; respiration is quicker, and there may be a little duskiness of the face and lips. The pulse quickens, varying from about 110 to 140, and may show an extreme degree of dicrotism. The first sound of the heart loses its muscular tone and comes to resemble the second sound. The blood-pressure progressively falls, the systolic pressure being usually below 100 mm. Hg. Towards the end of the week delirium is not infrequent. It is usually of a low muttering character but may become

noisy. Deafness is common, and sometimes repeated epistaxis occurs. In the second week the temperature remains at a high level—103° F. or so—but shows slight morning remissions, assuming the form of a plateau.

At the beginning of the third week the symptoms are at their height, *Third week* and, in favourable cases, gradual improvement is to be expected; but in severe infections it is during this week that serious complications occur, such as severe haemorrhage or perforation, or the sick man may pass into what is called the typhoid state. This is only seen in very *Typhoid* severe cases: the patient becomes utterly helpless and is unable to turn *state* in bed, lying on his back in a state of stupor or low muttering delirium. Profound nervous disturbance is shown by trembling of the hands and tongue, twitching of the tendons (subsultus tendinum), aimless picking at the bed-clothes or at the lips and nose (floccilatio, carphology), and relaxation of the sphincters with incontinence of urine and faeces. In some cases retention of urine occurs. Emaciation progresses and it is difficult to prevent bed-sores. Extreme abdominal distension may supervene and the patient may die in a state of coma or from intestinal perforation or haemorrhage. Yet in these cases a fatal ending does not always ensue, and, after prolongation of the fever for another two or three weeks, gradual recovery may take place. In the more usual type of case the third week witnesses a progressive fall in the morning temperature, the evening fall following more slowly. Thus, the temperature chart shows a remittent type of fever for a period of four days or so, followed by four days of an intermittent pyrexia ushering in the convalescent period. During the third week diarrhoea usually becomes more severe and there may be six or eight motions in the 24 hours. These may increase to twelve or twenty a day when extensive ulceration of the large bowel co-exists. Inspection of the stools may show sloughs which have separated from the inflamed Peyer's patches, and blood in macroscopic quantity may be seen. Improvement is shown by the tongue becoming cleaner, the output of urine larger, the motions more formed, the mind clearer, and sleep more peaceful.

In the typical case the fourth week is signalled by the achievement of *Fourth week* convalescence. The temperature is at first subnormal, though unstable, but sometimes it keeps up throughout the whole of the week. The pulse-rate may be slow, but it is often rather fast and, like the temperature, easily disturbed. The appetite becomes sharp and even ravenous. The weight rapidly increases. The feet and ankles may show slight oedema. Convalescence is liable to be interrupted by many mishaps, among which may be mentioned femoral thrombosis, 'typhoid spine', tenderness of the toes, bone abscesses, cystitis, and relapses. There is sometimes considerable temporary loss of hair.

Relapses occur in about 10 per cent of cases. They are most frequent *Relapses* about a week or ten days after the temperature has regained its normal level. They are probably due to the mobilization of typhoid bacilli which have been lying latent in some part of the body less readily accessible

to the specific protective substances. A re-infection of the blood stream takes place and subsequent re-invasion of the lymphoid tissue of the intestine. Mild attacks are more likely to be followed by relapses than are more severe ones which appear to confer a greater degree of immunity upon the patient. The relapse is usually shorter and milder than the original attack, but sometimes ends fatally. In the relapse all the symptoms recur, the rose spots make their appearance once more and at an earlier period, the spleen enlarges, and the intestinal lesions and mesenteric glands go through another cycle of change. The onset is more sudden than in the original attack and is often attended by a rigor. The fever more quickly reaches its maximum, and defervescence usually starts before the end of the second week. As many as five relapses have been recorded after an attack; one case of mine proved fatal on the 72nd day, during the third relapse.

Recrudescences In addition to the relapses during convalescence, intercurrent relapses, or recrudescences as they are more properly termed, may take place before the temperature has fallen to normal; they are manifested by an exacerbation of the pyrexia and febrile symptoms, and a fresh crop of rose papules. In this way indefinite prolongation of an attack of typhoid becomes possible.

Blood picture During the course of typhoid fever a progressive hypochromic anaemia takes place. In severe cases the red blood corpuscles may be reduced to one million per cubic millimetre, and after haemorrhage even lower counts may be recorded. Sometimes a wrong impression may be gained from a blood count, for in cases of severe diarrhoea dehydration may lead to such a degree of concentration of the blood that the anaemia may be obscured. The white count is characteristic—leucopenia with a relative lymphocytosis; leucocytosis points to a complication.

Types of typhoid The great variability in the clinical manifestations and course of typhoid fever has led to the description of special types of the disease. An ambulatory form is sometimes seen in which the patient may keep about during the first two weeks or so of his illness. The latter period of the illness in such cases is frequently calamitous and a tragic ending often supervenes. Mild and abortive forms occur in which the fever terminates rapidly during the second week. An apyrexial form is described. In the pneumonic form the attack may begin abruptly with signs of pulmonary consolidation, and the true nature of the disease may not be recognized, though in other cases as the pneumonia subsides the fever may run its typical course with intestinal disturbance, rash, and splenic enlargement. Meningo-typhoid and nephro-typhoid imply the existence of meningeal or nephritic symptoms at the onset of the disease and lead to difficulties in diagnosis in the early stage.

In the haemorrhagic form bleeding takes place from various mucous membranes, and petechiae and purpuric patches appear on the skin. A septicaemic type without intestinal lesions is very rare.

(5)—Complications

The most important complications of typhoid fever are those conse-
quent upon intestinal ulceration, namely, haemorrhage and perforation.
They most commonly coincide with separation of the sloughs in the
latter half of the third or the early part of the fourth week. Less com-
monly, they occur during convalescence when healing of the ulcers has
been retarded. In both haemorrhage and perforation there is usually a
sudden fall of temperature, and in the case of perforation, though not
constantly, pain usually attends its onset.

(a) Haemorrhage

Haemorrhage occurs in from 5 to 10 per cent of the cases. It may vary
in amount from a few fluid drachms to several pints and may be re-
peated. When copious it causes an abrupt fall in temperature, pallor,
increased rapidity or imperceptibility of the pulse, collapse, restlessness,
sighing respiration, and thirst, combined eventually with the passage of
blood. The spleen may shrink perceptibly. In some cases the haemor-
rhage is so great that death may occur before any visible sign is seen in
the stools. The blood may be either bright or dark, depending upon the
length of time it has been retained in the bowel before evacuation. It is
often clotted. Haemorrhage may precede intestinal perforation. Haemat-
emesis is very rare.

(b) Perforation

This, the most dreaded complication of typhoid fever, occurs in about
3 or 4 per cent of cases and is responsible for one out of every three or
four deaths. It is most common about the twenty-first day, but has been
seen as early as the second week and as late as the seventh. It is heralded
by sudden pain, usually in the right iliac fossa, accompanied by localized
tenderness, localized rigidity, and immobility of the abdominal wall.
Its onset is often attended by shivering and a sudden fall of temperature,
though this is not invariable. The pulse becomes increasingly frequent
and small. Other initial symptoms that may occasionally be noticed
are vomiting, the passage of one or two loose stools, or frequency of
micturition. The face often assumes an anxious expression and becomes
pallid or slightly grey. The sufferer often lies with his knees drawn up
and is unwilling to move. After recovering from the shock the patient
appears to be better for an hour or two, but the improvement is de-
ceptive and short-lived, for, after a few more hours, signs of a more
generalized peritonitis show themselves. Pain and tenderness are now
experienced all over the abdomen, distension increases, rigidity becomes
more general, bilious vomiting sets in and perhaps hiccup, and the
Hippocratic facies, pinched, drawn, and ashy, makes its appearance.
Death usually occurs within 48 hours.

The diagnosis of perforation may be difficult; the catastrophe has *Diagnosis of*
sometimes been diagnosed when it has not taken place, but more com- *perforation*

monly it has occurred without recognition. In the former event pain from some other cause has been wrongly attributed to perforation; in the latter the exhausted condition of the patient appears to delay the ordinary reaction of the peritoneum to irritation, or the patient may be in the typhoid state and in too stuperose a condition to be aware of painful impressions. Whichever is the case, it is important to realize that perforative peritonitis may begin insidiously and remain undetected. In such cases the chief indication may be increasing abdominal distension and deepening prostration. The distension is usually due to inflation of the paretic intestines, but sometimes a considerable quantity of gas escapes into the peritoneal cavity and leads to obliteration of the liver dullness. In flatulent distension of the bowel apart from perforation, the liver is more likely to be displaced upwards unless, as sometimes happens, the distended colon insinuates itself in front of the liver. On account of this possibility, absence of liver dullness is of much greater significance as a sign of perforation in those cases in which the abdomen is retracted.

Signs preceding perforation

Ker pointed out that there may be pain for two or three days before perforation occurs and that in many instances the temperature runs in a straight line without much remission for a day or two before its occurrence. He emphasized the importance of the daily examination of the abdomen in order to gain a thorough acquaintance with its condition, so that sudden changes might be the more readily appreciated, changes which in less carefully watched cases might be missed or disregarded. In not a few instances perforation is preceded by haemorrhage. The perforation

Site

usually occurs within the last two feet of the ileum and often close to the ileo-caecal valve, but it may occur in the caecum, vermiform appendix, or colon.

Blood picture in perforation

A polymorphonuclear leucocytosis follows infection of the peritoneum and may rise hour by hour, but, as it is also seen in other conditions associated with abdominal pain, too much weight must not be given its occurrence in arriving at a diagnosis of perforation.

Differential diagnosis of perforation

The chief complications which may simulate perforation are acute cholecystitis and perforation of the gall-bladder, suppurative adenitis of mesenteric glands, appendicitis, splenic infarction, and rupture of the spleen. Acute pneumonia with pleurisy may produce pain referred to the front of the abdomen, and abdominal rigidity may be present, but careful examination of the chest should prevent error.

(c) *Tympanites or Meteorism*

This, when great, is a most unfavourable symptom. The abdomen becomes ballooned and very tense. When present in high degree it betokens a high grade of toxaemia. The poisoned nerve-endings are no longer able to control the tone of the intestinal musculature, and distension of both small and large intestine takes place. It embarrasses the respiration and increases the risk of perforation by stretching the intestinal wall. Lesser degrees are predisposed to by an injudicious dietary.

(d) Ulceration of the Colon

In some cases the solitary lymphoid follicles are involved throughout the colon, which is then the seat of multiple circular ulcers. The condition is marked by intense diarrhoea, perhaps twelve or more actions in the 24 hours, and sleep may be seriously interrupted. The motions contain much mucus and are very offensive. When the rectum is involved in the ulcerative process painful tenesmus occurs. Tenderness may be found along the course of the colon and haemorrhage and perforation may occur.

(e) Myocardial Degeneration

The most common cause of death is gradually developing cardiac weakness. This is ascribed to the effect of toxaemia upon the myocardium. The muscle wall becomes weakened and the cavities show some degree of dilatation. When this occurs the first sound loses its *Heart sounds* muscular tone and becomes short and rather sharp like the second, and, as the change becomes more marked, a systolic murmur due to dilatation of the mitral orifice becomes evident. There is also shortening of the diastolic interval so that tic-tac rhythm becomes noticeable. The cardiac impulse becomes enfeebled, and it may be possible in some cases to make out some increase in the area of cardiac dullness. Gallop rhythm is of unfavourable significance. Intracardiac thrombosis sometimes occurs. The weakened power of the heart especially involves the pulmonary circulation, leading to congestion and oedema of the posterior and lower part of the lungs. More rarely a true myocarditis occurs, and malignant endocarditis has occasionally been recorded. Pericarditis is rare.

(f) Pulmonary and Vascular Complications

Bronchitis and hypostatic congestion of the lungs have already been referred to. Lobar pneumonia may arise in the third or fourth week of the fever. Both typhoid bacilli and pneumococci may be found in the sputum. The condition may fail to be recognized unless the chest is examined, as, although the respiration and pulse-rate are quickened, cough is often slight and rusty sputum may be absent. Streptococcal broncho-pneumonia is sometimes a terminal infection. Infarction, abscess formation, gangrene, and pneumothorax are rare.

Ulceration of the larynx is usually shown by hoarseness of the voice, *Ulceration of* inspiratory stridor, and the expectoration of blood-stained mucus, and *larynx* deglutition may be painful. Necrosis of the cartilages is usually followed by death. Thrombosis of the femoral vein is not very uncommon; it *Femoral* usually affects the left side. Pain in the calf or thigh may precede by a *thrombosis* day or two the recognition of the cord-like swelling of the vein. It is attended by a rise of temperature and by oedema of the foot and leg on the affected side. Pulmonary embolism may occur from detachment *Pulmonary* of the clot, but fortunately this is infrequent. Sometimes permanent *embolism*

enlargement of the leg may occur. Thrombosis most commonly appears during convalescence, but it may arise during the febrile period. Thrombosis of the internal jugular vein has been recorded. Arteritis with thrombotic occlusion is rare; it is manifested by pain, cessation of pulsation, and coldness of the limb. If a collateral circulation is not established gangrene will follow.

(g) Cholecystitis

This complication occurs in rather less than 2 per cent of cases. It is recognized by pain, tenderness, and rigidity below the right costal margin. Its onset may be sudden, accompanied by shivering and vomiting, and, as in perforation, the pulse-rate is increased and leucocytosis occurs. It must be distinguished from intestinal perforation arising in the febrile period. An icteric tinge in the conjunctiva or frank jaundice occurs in a third of the cases and enlargement of the gall-bladder is sometimes palpable. The symptoms usually subside and operative treatment is seldom necessary. Cholecystitis may supervene months afterwards as a sequel of the infection and lead to cholelithiasis, bile being favourable to the growth of the typhoid bacillus. Jaundice apart from cholecystitis is excessively rare. It appears to be of the toxic type due to changes in the parenchyma of the liver (Widal). The occurrence of cholecystitis increases the likelihood of the patient becoming a carrier.

(h) Parotitis

Parotitis may occur in severe cases. It is usually unilateral. When suppuration occurs typhoid bacilli may be recovered from the pus, and it may be attended by cellulitis or thrombosis of the jugular vein. It is of serious import.

(i) Urinary Tract Infections

Nephritis   Albuminuria due to cloudy swelling of the renal parenchyma is very common, but true nephritis with blood and epithelial casts in the urine is rare. A case associated with nephritis from the onset is sometimes spoken of as nephro-typhoid and uraemia not infrequently leads to a fatal termination.

Bacilluria   Bacilluria due to the presence of *B. typhosum* and characterized by the passage of turbid opalescent urine is not uncommon. More rarely there may be an associated pyelitis or pyelonephritis manifested by rigors, pyrexia, pain and tenderness in the lumbar region, and pyuria. Such cases may become urinary carriers. In a case recently under my care a rise of temperature during convalescence was due to a colon bacilluria and quickly subsided under treatment with alkalis.

(j) Lesions in Bones and Joints

Periostitis   Lesions of the bones are not infrequent sequelae to an attack of typhoid fever. Periostitis is the most common and may arise during the attack, as in a case referred to by Osler of a boy admitted to hospital in the

second week of typhoid with acute periostitis of the frontal bone
and of one rib. It is, however, commoner during convalescence,
being manifested by swelling, redness, pain and tenderness over the
affected bone. Recovery is usually rapid, but the condition may recur,
especially if associated with osteitis or osteomyelitis. In the latter event
infection may remain latent for many months or years, giving rise
after that time to abscesses from which the *Bacterium typhosum* can be
obtained. The long bones of the extremities are most often involved,
and of these perhaps the tibia is the commonest site of election. The
ribs and clavicles are also not infrequently affected. This complication
usually appears as a tender circumscribed swelling of the bone, and its
onset is usually unattended by pyrexia or constitutional disturbance.
The inflammation is chronic and relapsing, and, although resolution
may take place without suppuration, in the majority of cases abscess
formation occurs and typhoid bacilli may persist in the discharge for
long periods, so that persons affected in this way form a special group
of carriers.

'Typhoid spine' appears to be related to these bony inflammations, *'Typhoid*
but suppuration does not occur. Two types are recognized: (1) Osteo- *spine'*
myelitis affects the body of a vertebra and, through the production of
bony osteophytes and bony changes in the intervertebral discs, ankylosis
results between the involved vertebra and its neighbours on each side.
This isolated bony ankylosis usually affects the lumbar or lower dorsal
region of the spine and is attended by pain and tenderness, usually
referred to as lumbago by the patient. The intervertebral discs on X-ray
examination appear as dense as the vertebral bodies themselves and
osteophytes are seen. After some months with appropriate treatment
some degree of resolution appears to take place. (2) Widespread ossifica- *Generalized*
tion both of the spinal ligaments and often of the intervertebral discs *ankylosis*
occurs with the production of 'poker back'. The spine becomes encased *'poker back'*
in bone, but osteophytes are not shown by radiological examination. Pain
is not prominent, but the rigidity is permanent and no treatment is of
any avail. (See also ARTHRITIS. Vol. II, p. 105.)

Arthritis of large joints is rare; occasionally a painless effusion into *Arthritis*
the hip-joint, if unnoticed, may lead to spontaneous dislocation of the
hip.

(k) Skin

Bed-sores may lead to pyaemia or septicaemia, and boils and abscesses
may occur.

(l) Nervous System

Nervous complications are comparatively rare. In the so-called *Meningo-*
meningo-typhoid, initial symptoms may simulate tuberculous menin- *typhoid*
gitis or cerebrospinal fever. The cerebrospinal fluid is usually clear, with
little alteration in the cell and albumin content, and cultures remain
sterile. The condition is one of meningismus rather than meningitis. A
true meningitis may arise during the third week, typhoid bacilli being

found on cerebrospinal puncture. The cerebrospinal fluid may be clear or turbid. Cases also occur of suppurative meningitis due to secondary infection. The cerebrospinal fluid is purulent and may show streptococci, staphylococci, or pneumococci, with or without typhoid bacilli. Such cases are always fatal. Hemiplegia is rare and is more likely to be due to *Cerebral abscess* thrombosis than to embolism. Cerebral abscess may be either secondary to an otitis media or to a pyogenic focus elsewhere; these abscesses, however, are usually due to a secondary invader and only rarely to the typhoid bacilli. Abscesses without an obvious primary focus sometimes occur and from these a pure culture of *B. typhosum* may be obtained.

Other nervous complications Myelitis with paraplegia, an ascending paralysis of the Landry type, and bulbar palsy have been recorded. Double optic neuritis, and peripheral neuritis affecting either a single nerve, such as the ulnar, or multiple nerves, are also sometimes seen. The most common form is a polyneuritis involving the feet and causing tenderness of the toes. The prognosis in neuritis is good.

Mental symptoms Mental symptoms are not very uncommon. Acute toxic confusional states occur during the febrile period, and post-typhoid insanity of many forms, the nature of which depends on the psychological constitution of the patient, are encountered from time to time.

(m) Inflammatory Complications

Lastly, some inflammatory conditions may arise during the course of typhoid fever such as orchitis, prostatitis, vulvitis, mastitis, and suppurative otitis media.

(6)—Prognosis

Death-rate Of cases ending fatally two-thirds die from toxaemia and one-third from complications arising in the course of the disease. The death-rate varies so much in different localities and in different epidemics that it is not easy to arrive at an average figure, but perhaps 15 to 20 per cent is a fair estimate. Age has a decided influence; except in infants the mortality under 10 years of age is low, after which there is a steady increase as years advance. The existence of previous organic disease, obesity, great muscular development, privation, and alcoholism are unfavourable. If in 'ambulatory' typhoid treatment is delayed and the patient is exhausted by activity during the first week or two of the disease, the outlook is very grave. Unfavourable features of the attack are persistent diarrhoea, tympanites, stupor, prolonged muttering delirium, muscular twitchings, a pulse-rate persistently over 120, indications of heart failure, cyanosis, and hypostatic congestion of the lungs.

Effect of complications on prognosis Of the many complications perforation is the most serious, and without operative intervention it is almost always fatal. When operation is undertaken early about one case in every four may be expected to recover. Haemorrhage, while seldom directly fatal, makes ultimate recovery much less likely. Repeated loss of small amounts of blood for several days is a very serious omen. Indeed experience has shown that after a profuse haemorrhage recurrence is less likely.

In a small number of cases sudden death occurs, preceded in some *Sudden deaths* instances by an attack of sudden dyspnoea, fainting fits, or irregular pulse. The end of the third week is the most usual time for this to happen, but it may occur during convalescence. In some cases no obvious cause has been found and adrenal failure has been postulated. In others sudden death has been due to pulmonary embolism, thrombosis of the pulmonary artery, or myocardial degeneration.

Relapses are rarely fatal, but perforation may occur, and when relapse *Relapses* follows relapse death may occur from exhaustion.

Typhoid contracted during pregnancy frequently leads to abortion or *Prognosis during pregnancy* premature delivery, and if the foetus is not dead it usually succumbs to the typhoid infection.

(7)—Diagnosis and Differential Diagnosis

There is little doubt that the charm of clinical diagnosis in infective conditions has largely waned since the application of bacteriological methods to the investigation of fever. Be this as it may, the only absolute proof that a person is suffering from typhoid fever is the isolation of *B. typhosum* from the blood, and only less infallible is the presence in *Isolation of organism* the blood of specific agglutinins. For the investigation of a suspected case of one of the enteric fevers a fair quantity of blood must be *Blood culture* withdrawn, as the bacilli are present in comparatively small numbers; ten to twenty c.c. of blood are taken from a vein and added, preferably at the bedside, to 50 or 100 c.c. of broth containing bile-salts or sterilized ox-bile, since so great is the bactericidal action of undiluted blood that if the blood is not diluted the growth of bacilli is hindered; and the presence of bile or bile-salts favours the growth of these organisms, mainly by diminishing the growth of contaminants. Even after as short an incubation as six hours it is often possible by putting up a hanging-drop preparation to detect the presence of a motile organism, and if smears are then made upon a solid medium, such as agar, it will be possible to obtain sufficient growth for an agglutination reaction to be carried out with typhoid and paratyphoid antisera some hours later. At the same time sugars may be inoculated for the further study of the biochemical characteristics of the organism.

Blood culture is especially valuable as a means of early diagnosis, as it is possible to isolate the infecting organism within the first few days of the disease. The percentage of successful cultures begins to fall after *Agglutination reactions* the first fourteen days, but by this time, in the vast majority of cases, specific agglutinins will have formed to such an extent that, when the patient's serum is put up against fresh laboratory cultures of *B. typhosum* and *B. paratyphosum*, Widal's agglutination reaction will be obtained without difficulty. For details both as to the methods employed in carrying out these tests and the significance of the findings reference should be made to the agglutination tests, Vol. II, p. 487.

If the organism has not been obtained from the blood, specimens of urine and faeces should be examined, no reliance being placed on a

Isolation of organism from urine and faeces

single negative culture. After the end of the second week bacilli are recovered more frequently from the excreta than from the blood. Some bacteriologists have obtained the organism from the faeces in 50 per cent of cases examined in the first week, a percentage increased to more than 75 in the third week. The bacillus is rarely recovered from the urine before the tenth and often not before the fifteenth day.

Blood count

A blood count is often a valuable help in diagnosis; the enteric group of fevers is characterized during the second week by leucopenia with a relative lymphocytosis, but this is not invariable as is illustrated by a case recently seen on the twelfth day in which the leucocytes numbered 13,000 per c.mm. with 70 per cent of lymphocytes. An average count is 3,000 to 5,000 or 6,000 leucocytes per c.mm. with about 50 per cent of lymphocytes. A case of ordinary severity often shows a polymorphonuclear increase during the first week, but in severe toxic cases leucopenia and relative lymphocytosis may be present from the outset. The appearance of a polymorphonuclear leucocytosis accompanies the onset of inflammatory complications.

When laboratory aid is not available Marris's test or Ehrlich's diazo reaction may furnish confirmatory evidence.

Marris's test

Marris's test depends upon the fact that in the enteric fevers atropine fails to accelerate the pulse-rate to the degree seen in other infections or in normal individuals. Atropine sulphate $\frac{1}{50}$ grain is injected hypodermically, and the pulse-rate, taken during the period of 25 to 50 minutes following the injection, is compared with that taken immediately before the injection was given. In fevers other than those of the enteric group the pulse-rate during the above-mentioned period exceeds the pre-injection rate by 30 or 40 beats per minute, whereas in the enteric fevers the rate is practically uninfluenced, increasing by not more than 10 beats. Readings between 10 and 20 are uncertain.

The test is very convenient for use in the tropics. It is of most value in the second week of the disease and a normal response may be resumed after the fourteenth day. The test may fail in persons over 50 years of age, especially if arteriosclerotic changes are present.

Diazo reaction

Ehrlich's diazo reaction. To a few c.c. of urine in a test-tube an equal quantity of a saturated solution of sulphanilic acid in a 5 per cent dilution of strong hydrochloric acid is added, and 2 or 3 drops of a 0·5 per cent solution of sodium nitrite are next added. By shaking a froth is induced, and a few drops of strong solution of ammonia are allowed to trickle down the side of the tube. The reaction is positive if the liquid becomes crimson and the froth assumes a rose-pink colour. The reaction appears between the fourth and tenth days and persists during the height of the fever.

The value of the reaction is somewhat impaired by the fact that it is not peculiar to the enteric fevers, as it may be found in measles, scarlet fever, pneumonia and tuberculosis; but measles, the only disease in which it is present with any great frequency, is seldom likely to be mistaken for typhoid.

Apart from laboratory diagnosis it may be said that *in temperate*

countries a fever which lasts a week without falling on any occasion to
normal, and without the appearance of any characteristic rash or any local
inflammation, is nearly always one of the enteric group. Some exceptions
will readily come to mind, such as undulant fever, Malta fever, some
cases of tuberculosis, and some cases of lymphadenoma.

In view of the help now afforded by laboratory investigation, the
diagnosis of typhoid has been simplified enormously, and it will not be
necessary to deal at length with the various diseases which may cause
difficulty. When epistaxis or severe headache or mild bronchitis or diar-
rhoea is associated with a rising pyrexia lasting a few days, the possibility
that the case is one of typhoid fever must be borne in mind. If in addi-
tion disturbed action of the bowel—diarrhoea or constipation—is
associated with abdominal discomfort and slight distension, the proba-
bility becomes increasingly great. Relative slowness of the pulse and
the presence of dicrotism would be additional evidence. The appearance
of rose spots and splenic enlargement after pyrexia of a week's duration
will confirm the diagnosis. Primary uncomplicated bronchitis is not
likely to give rise to a temperature exceeding 101° F., and in those cases
of bronchitis in which a higher temperature occurs it either indicates
the coexistence of broncho-pneumonia or that the bronchitis is really
secondary to some underlying cause, such as typhoid.

The diseases most frequently mistaken for typhoid are pneumonia,   *Differential*
broncho-pneumonia, influenza, acute miliary tuberculosis, tuberculous   *diagnosis*
meningitis, tuberculous peritonitis, malignant endocarditis, undulant
fever, typhus fever, psittacosis, and tularaemia.

A deep-seated pneumonia may simulate typhoid, and it may be some   *From*
days before the physical signs are conclusive; but pneumonia has usually *pneumonia*
a much more abrupt onset, and it is unusual for the respirations to be
less than thirty a minute, a rate seldom reached in the early stages of
typhoid. Cases of typhoid, however, occasionally present prominent
respiratory symptoms, and these may lead to the underlying infection
being overlooked. The presence of labial herpes is in favour of pneu-
monia, though it is sometimes seen in paratyphoid, and a leucocyte
count would probably exclude the likelihood of typhoid, as leucocytosis
is so rarely absent in pneumonia, whereas a leucopenia with relative
lymphocytosis would almost negative pneumonia. Careful and repeated
physical examination of the chest should never be omitted in doubtful
cases. As the two diseases may coexist a positive blood culture would
set the matter at rest.

Broncho-pneumonia in children, especially if attended by abdominal   *From*
distension and diarrhoea, is not infrequently mistaken for typhoid, and *broncho-*
further difficulty is added by the fact that in children with typhoid the *pneumonia*
rash is quite commonly absent. In broncho-pneumonia, however, there
is a much higher respiratory rate, with typical grunting expiration and
post-inspiratory pause, and active alae nasi, even when physical signs
continue to be indefinite. The spleen seldom shows the marked enlarge-
ment found in typhoid, and the tendency to cyanosis is much greater.

A minor sign well worth attention is the peculiar brown discoloration of the palms of the hands sometimes present in children with typhoid.

Influenza may simulate typhoid by the presence of high fever, bronchial catarrh, epistaxis, diarrhoea, and delirium. Apart from pulmonary involvement it is exceptional for the pyrexia to remain high for a week or longer. Pain in the back and limbs is more in evidence. A relatively slow pulse may occur in either condition, but the presence of dicrotism would be in favour of typhoid. Later the splenic enlargement and the eruption of rose spots would settle the diagnosis.

Acute miliary tuberculosis is perhaps the disease in which the greatest difficulty is met with in the differential diagnosis of typhoid fever unless a blood culture is carried out in the early stages. It may simulate typhoid in its insidious onset with malaise and headache, its rising fever with morning remissions, its relatively slow pulse, bronchitis, and possible enlargement of the spleen. The temperature, however, in miliary tuberculosis is more irregular, and may be of the inverse type, i.e. higher in the morning than in the evening, sweats are more frequent and cyanosis quickly becomes pronounced, the alae nasi show active movement, the respiratory rate is more rapid, and râles often crepitant in character are audible over the lungs. The presence of typical spots in the one case or the recognition of tubercles in the choroid in the other would decide the question; but in the absence of these, Widal's reaction may be the only impersonal method of diagnosis possible.

Tuberculous meningitis is differentiated by the presence of repeated vomiting, convulsions, and the persistence of headache after delirium is established. Retraction of the abdomen would be strongly in favour of meningitis but a tumid abdomen is sometimes seen. Kernig's sign and retraction of the head, if well developed, would strongly favour a diagnosis of meningitis, but on account of the presence of muscular rigidity in some cases of typhoid (meningo-typhoid) too much emphasis must not be placed on these signs unless well developed. Lumbar puncture will, of course, settle the question. In cases of tuberculous meningitis the cerebrospinal fluid would show an increase in lymphocytes and a reduction of chlorides and sugar, and the fluid would be under pressure.

More rarely tuberculous peritonitis on account of its slow onset, continued fever, and abdominal distension may be mistaken for a mild attack of typhoid. The presence of caseous masses in the abdomen or the development of ascites or pleural effusion would make the diagnosis clear.

Malignant endocarditis, on account of its continued high temperature and splenic enlargement, has occasionally caused difficulty in diagnosis. Careful physical examination of the heart, of the skin for petechiae, and of the urine for traces of blood (embolic nephritis) usually enables the diagnosis to be made. Blood culture may be extremely valuable.

Undulant fever may be diagnosed as typhoid in the early days of the disease, but there are fewer manifestations of toxaemia, and as time goes on muscular and arthritic pains come into prominence, drenching sweats

are experienced, and the characteristic remissions make their appearance. Blood culture may lead to the detection of the causal organism, and agglutination reactions against the *Brucella abortus* are given in high titre.

In tropical countries malaria sometimes gives rise to a continuous type *From* of fever which may suggest typhoid; the detection of malarial parasites *malaria* in the blood enables the distinction to be made. When malaria and typhoid coexist in the same patient, positive agglutination reactions against *B. typhosum* will help to make the diagnosis clear.

In countries where typhus occurs it will be important to distinguish a *From typhus* mild case of typhus fever from typhoid and a severe case of typhoid fever from typhus. The points in favour of typhus are the sudden onset, the higher range of temperature during the first few days and its less remittent type, the dull, heavy aspect, the contracted pupils and injected conjunctivae, the absence of abdominal distension and diarrhoea, and the greater tendency to delirium and stupor. The rash appears earlier in typhus, and in addition to the petechial eruption there is definite subcuticular mottling.

Appendicitis has been diagnosed in the early stages of what is really *From* typhoid fever; the surgeon sometimes becomes aware of his error by *appendicitis* the temperature failing to fall after the appendix has been removed. Although tenderness in the right iliac fossa is often present in typhoid, it is rarely so marked or so localized as in appendicitis, and the presence of leucopenia would strongly discountenance a diagnosis of appendicitis. A similar blood finding would also serve to exclude another difficulty, namely deep-seated pus formation; and rigors, though they do sometimes occur, are not likely to be met with in typhoid unless some complication, such as cholecystitis, phlebitis, or perforation, has arisen.

Psittacosis presents exceptional difficulties both from the clinical and *From* serological aspects. A story of intimate contact with a sick parrot or *psittacosis* love-bird can usually be obtained and due regard must be paid to such evidence in arriving at a diagnosis. Clinically the resemblance to typhoid may be singularly close, for not only may the onset of pyrexia be associated with headache, epistaxis, and bronchial catarrh, but later the patient becomes languid and apathetic, and abdominal distension and an eruption of rose spots may appear. Attention must be paid to the fact that the initial rise of temperature is abrupt in psittacosis, the spleen cannot be felt, and the rose papules when present are smaller than those seen in typhoid. From the serological aspect further difficulty arises from the fact that in some cases Widal's agglutination reaction to the *B. typhosum* has been positive for typhoid. Such a reaction has been obtained early in the course of psittacosis in high dilution, a state of affairs quite unlikely to be met with in typhoid, but typhoid bacilli cannot be grown from the blood. Signs of pulmonary involvement are nearly always present in psittacosis, and when sputum can be obtained it may be possible to prove the presence of the virus of the disease by injection into white mice (Rivers and Berry).

From tularaemia　In countries where tularaemia is endemic cases occur closely resembling typhoid fever, but it is possible to establish the diagnosis by a positive blood culture or agglutination of the *Brucella tularensis*.

From other conditions　I have known cases of phlegmonous gastritis, pyogenic abscesses of the psoas muscle (non-tuberculous), unrecognized long-standing empyema, and trichiniasis mistaken for typhoid fever. In the last-mentioned instance, chemosis of the conjunctiva led to the recognition of the disease, which is also characterized by a high grade of eosinophilia.

(8)—Treatment

(a) Prophylaxis

Vaccine　A vaccine containing 1,000 million of dead *B. typhosum* and 750 millions each of *B. paratyphosum A* and *B* per c.c. is in common use. The first dose consists of 0·5 c.c., the second dose consists of 1 c.c. given a week or ten days later, and sometimes after another week a third dose of 1 c.c. is given. The vaccine is administered by deep injection into the flank or deltoid region. Persons intending to reside in the tropics or to visit countries where typhoid is rife are wise to seek immunization, but protection is not absolute, and they must take all the usual precautions to avoid infection. Immunity is usually considered to last for a year or two. Those taking up fever nursing should be inoculated for their own protection (see IMMUNITY AND IMMUNIZATION).

(b) Treatment of Attack

Isolation　As soon as the diagnosis of typhoid fever becomes probable the patient should be isolated and strictly confined to bed. A bed-pan and urine **General** glass are essential. The bed should be narrow with an elastic mattress, **measures** and a large piece of waterproof should be placed below the cotton or linen sheet. A water-bed is not necessary. The temperature of the room should not exceed 60° F. In summer or in hot countries the windows should have fly screens. The patient should be lightly covered with a sheet and thin coverlet, a light blanket being placed over the feet unless the weather be very warm.

Disinfection of excreta and fomites　All discharges must be regarded as infective, and the stools, urine, and sputum should be mixed with excess of 1 in 20 phenol and allowed to stand for several hours before being thrown down a drain. When no drains exist they should be mixed with sawdust and turpentine and ignited. Earth-closets are not suitable for typhoid evacuations. Pyjamas and bed-clothes should similarly be soaked in 1 in 20 phenol for some hours before being sent to a laundry. The nurse cannot be too careful. Overalls should be worn and rubber gloves employed when giving enemas or handling bed-pans, and a rubber apron is useful when a child is being nursed. The hands too, whether gloves are worn or not, should be washed with plenty of soap and water after attending to the patient. Feeding utensils should be scalded after use and reserved for the patient alone.

Diet　The diet should be liquid and given every 2 or 3 hours, according to

the severity of the case. It is usual to allow 2 or 3 pints of milk in the 24 hours, and if diarrhoea is not a prominent feature of the case, 1 pint of beef tea or other solution of meat may be substituted for a pint of milk, and as much water as the patient desires may be taken between the feeds. Milk yields 20 calories an ounce, so that if milk alone be given, 5 pints would be required to yield 2,000 calories a day. Such a quantity would be too great to be taken with comfort, so its calorific value is usually increased by the addition of lactose, the least sweet of all the sugars. If the patient craves for sweets, glucose or glucose lemonade or powdered chocolate may be given. Weak tea, which is an excellent diuretic, may be allowed in small quantities at a time. When diarrhoea is troublesome arrowroot may be of service. Alcohol is not usually necessary, but if a patient has been accustomed to its use a moderate amount of brandy or whisky may be permitted. Great care is necessary during convalescence, and solid food should not be given till the evening temperature has been normal for several days. Relapses are more frequent when solids are resumed too early. A thin rusk or sponge-cake may be first allowed, and then a thin piece of bread and butter with a lightly poached egg, next a little boiled fish with perhaps 'riced' potato or potato purée, and, finally, a little tender meat.

During the acute period attempts must be made to control the pyrexia *Control of* by sponging. Whenever the temperature exceeds 102·5° F. the patient *fever* is sponged with water at 70° F. It takes about 20 minutes to sponge a typhoid patient efficiently, the limbs being sponged in turn and finally the body. If there is much collapse and cold sponging is greatly objected to by the patient, water at 110° F. may be used, which, by dilating the cutaneous capillaries, will lead to loss of heat if the patient is left lightly covered afterwards. Another method is to place a tin tray of ice a short distance above the patient and thus keep him continually in a bath of cool air. The good effects produced are by no means confined to the lowering of the temperature. The rate of the pulse is decreased and its tone improved; headache, insomnia, and delirium are lessened, and the *Contra-* amount of urine excreted is increased. This method is contra-indicated *indication* when haemorrhage has recently occurred.

Many drugs have the power of reducing temperature but on account *Antipyretics* of their depressant effect it is wise to avoid their use. An exception may be made in the case of quinine; 10 grains of quinine sulphate given once or twice in a single dose at the height of the fever in cases in which pyrexia is only controlled with difficulty is sometimes of definite service.

The care of the mouth is important; a piece of gauze or linen moistened *Cleansing of* with glycerin of borax wrapped round the finger of the nurse is an *mouth* excellent means of securing cleanliness, alternating with a solution of sodium bicarbonate, which aids in detaching sticky mucus. In severe cases one or other of these applications should be used every four hours, and the more water a patient is given the more satisfactory the state of the mouth and tongue is likely to be.

As regards drugs salol, 5 grains three times a day, serves to deodorize *Salol*

the stools by keeping down putrefactive and fermentative organisms,

Burney Yeo's mixture or the well-known Burney Yeo's mixture of nascent chlorine and quinine may be continued throughout the illness. This mixture is made by pouring 40 minims of strong hydrochloric acid upon 30 grains of powdered potassium chlorate in a 12-ounce bottle; water is added gradually, the bottle being corked and shaken after each addition in order to dissolve the nascent chlorine. When the bottle is almost full 24 grains of quinine hydrochloride are added. One fluid ounce of the mixture is given every 3 or 4 hours. Another favourite plan is to give

Cinnamon every 2 hours 3 or 4 minims of oil of cinnamon suitably diluted. It is safer not to give purgatives by the mouth after the tenth day, and when

Enemas constipation is present an enema should be given on alternate days. When the motions exceed four or five in the twenty four hours, opium

Opium may be administered either by mouth as Dover's powder or by the bowel in the form of a starch and opium enema. If there is much collapse the bed-pan should be dispensed with and the motions passed into a draw sheet.

Treatment of haemorrhage For profuse haemorrhage the chief indication is to keep the bowel at rest by withholding food for some hours, and by administering opium, which not only arrests peristalsis but prevents the patient from being unduly conscious of the deprivation of food and water. The best form is Dover's powder, 5 grains being given at once and repeated after an hour if the patient is not sleeping, after which it may be given at four or six-hourly intervals for a couple of days. In the event of a very profuse haemorrhage a hypodermic injection of morphine may first be given to ensure a more rapid action. If, after two days, there is no fresh blood in any stool that has been passed or if there has been no movement of the bowel, the opium may be stopped, and an olive-oil enema may be given if no action has occurred by the fourth day. The subcutaneous injection

Hemoplastin of hemoplastin in 2 c.c. doses on one or two occasions is another excellent means of controlling haemorrhage. Brandy in half-teaspoonful doses in order not to increase the blood-pressure unduly and so add to the risk of recurrence of bleeding is often a useful adjunct.

Saline If the patient appears to be in danger of sinking, 10 fluid ounces of physiological saline may be injected under the skin and repeated when

Blood transfusion necessary, or a small transfusion of blood from a suitable donor may be given. The latter procedure is indicated if the haemoglobin percentage falls below 40.

Treatment of perforation When perforation has occurred, unless the patient is already moribund, laparotomy should be performed without delay and the perforation closed by suture. The stitched perforation should be brought as near as possible to the wound and a rubber drain inserted into the peritoneal cavity. If at the time of operation perforation appears to be threatening in neighbouring ulcers they too should be sutured in a similar manner. Operation statistics show that the prognosis is rather better in cases of paratyphoid than in typhoid. If the perforation is not found in the last 18 inches of the ileum, the caecum and ascending colon should

be scrutinized before going further afield. Occasionally perforative symptoms are caused by rupture of an ulcerated gall-bladder.

Meteorism or paralytic distension of the bowel should always be regarded as a sign of the utmost gravity, and no time should be lost in attempting to obtain relief. Turpentine in 20-minim doses, either in almond mixture 1 drachm or suspended in a suitable amount of mucilage, should be given by mouth at two- or three-hourly intervals, and turpentine stupes should be applied to the distended abdomen. Kaolin poultice or antiphlogistin applied so as to cover the whole abdomen is sometimes attended by relief. The use of the rectal tube is admissible, and enemas of turpentine or oil of rue may be given. The diet should be reduced and food administered at longer intervals. If relief is not obtained the patient usually succumbs to toxaemia, if not to perforation. *Treatment of meteorism*

Circulatory failure is treated on general principles. Among the drugs in common use are strychnine, camphor preparations, adrenaline, caffeine, and ether. If thrombosis of the femoral vein supervenes the leg should be immobilized by means of sandbags, and extract of belladonna may be gently applied along the course of the affected vein. The intravenous injection of 5 to 10 fluid ounces of 0·5 per cent sodium citrate solution is usually attended by relief of pain, and from theoretical considerations it should diminish the likelihood of extension. *Of circulatory failure*

Bacilluria and cystitis usually respond to hexamine 10 grains, three or four times a day, a tumbler of water being given with each dose to avoid irritation of the urinary tract. Suppurative parotitis usually demands surgical intervention. Cholecystitis often subsides without operation. Periostitis should be treated by hot fomentations and, when suppuration occurs, by incision. The relapsing osteitis associated with abscess formation occurring as a sequel, perhaps years after an attack of typhoid, is usually treated by free incisions, any necrotic bone being removed. The infective nature of the pus must be borne in mind and the patient regarded as a carrier. *Of bacilluria, cystitis, and other conditions*

Headache is often benefited by 10 grains of aspirin or 5 grains of caffeine citrate. Some advise the constant use of an ice cap when it is very severe. When such measures as cold sponging and the administration of hot drinks fail to relieve insomnia, 20 grains of sodium bromide with 10 grains of chloral hydrate, followed when necessary by half the amount at half-hour intervals till sleep is secured, the pulse being carefully watched, is a satisfactory method of treatment. Dover's powder in 5-grain doses is also in common use for this purpose. *Of headache*

During convalescence the temperature remains in a very unstable state, and temporary febrile exacerbations may follow unsuitable food, constipation, or mental excitement. Strain and over-exertion should be avoided, as cardiac dilatation or even fatal syncope may occur. In the absence of any sequelae a patient may be allowed out of bed for a short period about ten days after the temperature has become normal. The urine and faeces should be submitted to bacteriological examination on two or three occasions during the period of convalescence. *Convalescence*

Negative results, however, afford no absolute guarantee of safety, because carriers may excrete typhoid bacilli intermittently. After an attack of typhoid the patient should always have a period of rest in the country or at some health resort before returning to his ordinary life.

Conclusion

It cannot be too strongly emphasized that during the acute stage of typhoid fever the patient must be seen daily by his medical attendant, who must make a daily examination of the abdomen. He will note the degree of distension, whether the bladder is being properly emptied, and whether the stools contain blood or curds, the presence of the latter indicating that milk is being imperfectly digested. He must see that the patient's position is changed from time to time in order to avoid the occurrence of hypostatic congestion. The temperature and pulse must be charted four-hourly and the nurse be directed to report at once any sudden drop in the temperature below the normal line or any sudden change in the pulse or the occurrence of a rigor. A note must also be kept of the daily intake of fluid and as far as possible of the amount of urine passed. Finally he must assure himself that the nurses in attendance are carrying out their duties with promptitude and intelligence. In no disease are a wise practitioner and competent nurses more essential.

(9)—Carriers

Temporary carriers

Individuals who recover from typhoid may continue to harbour the bacillus for months or years. Those retaining the bacilli up to the third month after convalescence are spoken of as convalescent or temporary carriers, and about 5 per cent of typhoid patients become temporary carriers. After this period of time any that still harbour the bacillus are

Chronic carriers

known as chronic carriers. About 2 per cent of typhoid patients become chronic intestinal carriers, a smaller number, urinary carriers. In both, the discharge of bacilli may be intermittent. Some suffer from periodic disturbances of the gall-bladder, bowel, or urinary tract, but many are

Healthy carriers

symptomless. Healthy carriers is the term used to designate those who are not known to have suffered from typhoid but are capable of infecting others. A well known case of a carrier is that of 'typhoid Mary', a cook who had lived in service in seven families during a period of years. In each family typhoid fever occurred, and twenty-eight cases in all were directly traced to her.

Treatment of carriers

The treatment of carriers is difficult and unsatisfactory. The best course is to make a carrier understand clearly in what way he is a danger to his fellows. Personal hygiene and care in the disposal of faeces, urine, and personal linen are of the utmost importance. Towels must be strictly reserved for his own use. No carrier must engage in the preparation or purveyance of food. Enormous doses of hexamine have been given in the hope of sterilizing the gall-bladder in the case of faecal carriers and smaller doses in the case of urinary carriers, but the results in both cases are disappointing. Nor can vaccines be relied on to abolish the carrier state. Excision of the gall-bladder should not be recommended indiscriminately, for, though some have been freed from their incubus,

a cure cannot be foretold, as in some cases the bile-ducts harbour the infection. Nor is the operation without risk; cholecystectomy and operations on the kidney have been followed by typhoid septicaemia. In special circumstances preventive inoculation of contacts may be advisable.

3.—PARATYPHOID FEVER

419.] Paratyphoid fever is clinically indistinguishable from typhoid and the diagnosis can be made by bacteriological and serological methods only. They are distinct diseases, and typhoid fever does not confer immunity against paratyphoid, and vice versa. Three organisms are usually described: *B. paratyphosum A, B,* and *C.* Paratyphoid A occurs especially in India and the East; paratyphoid B is more frequent in Europe, America, and in temperate climates; paratyphoid C occurs in the Balkans and is very rare in England. As in typhoid, the organisms can be grown from the blood, urine, and faeces of the infected person, and specific agglutination reactions are obtainable, but some infections with paratyphoid C fail to produce agglutinins. Leucopenia is less marked than in typhoid.

Paratyphoid B is usually milder than typhoid in its clinical manifestations, *Clinical* runs a shorter course, and has a lower mortality rate. The onset is often *picture* more abrupt and more likely to be attended by gastro-intestinal symptoms; thus diarrhoea is frequent and vomiting hardly less so. Shivering is sometimes evident. The temperature rises rapidly at the onset and may attain its acme by the third day, a day or two earlier than in typhoid - and after a plateau of seven or eight days, during which it shows a more marked daily variation, falls rather rapidly by lysis. Typhoid is *Duration* often regarded as a twenty-two days' fever; in contrast paratyphoid runs a course of sixteen days or so, though, as in typhoid, the fever may be prolonged by recrudescences and relapses.

Headache, apathy, enlargement of the spleen, and tumidity of the abdo- *Symptoms* men are usually present. Headache is often more severe than in typhoid, abdominal distension less so. Sweating is more frequent and herpes more common. An eruption of rose spots occurs about the seventh day and the individual papules may be larger and more profuse than in typhoid.

Pulmonary complications are mild, but bronchitis is usually present *Complications* and broncho-pneumonia may occur. Complications similar to those seen in typhoid are less frequent and less severe; this holds good as regards intestinal haemorrhage, which, when it does occur, is likely to be less severe; perforation is rare and the 'typhoid state' exceptional. Some cases closely resemble dysentery.

Paratyphoid A often runs a longer course than paratyphoid B and in it a positive Widal reaction is later in appearing. It is said that sufferers from paratyphoid A are more prone to become carriers.

The pathological changes produced in the body by the various enteric

Morbid changes

organisms are fairly uniform, but ulceration of the lymphoid tissue of the intestines is relatively less severe in paratyphoid fever. Ulcers may be more numerous in the colon and rectum than is the case in typhoid. Splenic abscesses are thought to occur with greater frequency and broncho-pneumonia appears to be more common.

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ENTEROCELE

See HERNIA

ENTROPION

See EYELIDS, INJURIES AND DISEASES, p. 239; *and* TRACHOMA

ENURESIS

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Reference may also be made to the following titles:

ALLERGY   CHILD HEALTH AND WELFARE
CHILD GUIDANCE   PSYCHONEUROSES

1.–DEFINITION

420.] Enuresis may be defined as an absence of control over the act of
micturition. It is not quite the same as incontinence of urine, the latter
term being usually applied to a more or less continuous 'dribbling', nor
is it necessarily associated with frequency of micturition. Certain age
limits must be introduced to modify this definition in its strictest sense,
for control over the evacuation of the bladder is only gradually acquired,
perfection being reached at a somewhat variable age. As a working
rule it is doubtful if the term enuresis should be applied to the child
under three years and the condition rarely persists after puberty.
Enuresis may be nocturnal, diurnal, or occur during both the day and
night: the first-named of these is the most common.

2.–CAUSATION

The exact aetiology of a given case of enuresis is often very difficult to
determine and, as will be pointed out, treatment is usually largely em-
pirical because of this difficulty. The age at which a child becomes 'clean'

in its habits, as already mentioned, is somewhat variable. Too strenuous efforts on the part of parents and nurses to train a young baby to pass its urine only into a receptacle may have the undesired effect of making what should be a natural reflex action into a sort of moral conflict. The effect of fear upon the emptying of the bladder is well recognized and it may well be that anxiety states and emotional upsets play a part in many a child with enuresis. It is well known that even the most persistent bed-wetter at home usually shows great improvement when moved to the more placid and better disciplined atmosphere of a hospital ward. This possible psychological background for the disorder must always be kept in mind, for it seems quite clearly established by the work carried out in the modern child guidance clinics that bed-wetting is a frequent sign of an unstable child reacting badly to environment and life as he finds it.

Training

It has already been mentioned that the age at which a child becomes 'dry' varies and great delay in the acquisition of clean habits naturally raises the question of the mentality of the patient. Generally speaking, nocturnal enuresis is more often associated with an intelligence which is above the average than with the minor degrees of 'backwardness', but the possibility of mental deficiency as an explanation for lack of bladder control must be kept in mind. Just as too much training, as already mentioned, may fail to achieve its object, so a complete lack of any training in bladder control may result in a persistence of the uncontrolled state into late childhood. The baby should be 'held out' at definite times and the older child made to go to the lavatory. Until a child is three years old at least, it should generally be roused when the parents go to bed and made to pass water. Failure to achieve any success with the training may mean that the mentality is at fault, but even with mentally deficient children dry habits can usually be attained in time.

Physical defects

Apart from these mental and psychological causes, there are in a few instances certain physical factors to be considered. Disorders of the urinary tract, such as an infected urine from pyelitis or cystitis, stone, nephritis, and the passage of a highly acid urine may be responsible for an increased irritability of the bladder or for a polyuria which leads to enuresis. Polyuria from other causes, such as diabetes, must also be excluded. Local infection of the lower end of the urethra or its neighbourhood, as in balanitis or vulvitis, may sometimes lead to involuntary passage of urine by a young child, but this is usually only of a temporary duration. It is very questionable if phimosis ever causes enuresis and, though it may be desirable to perform circumcision on other grounds, this operation should never be relied on to 'cure' bed-wetting. Intestinal worms, constipation, and proctitis are all doubtful causes of the bladder trouble but if present should certainly be treated on general grounds. It is equally doubtful if enlarged or diseased tonsils and adenoids can play any part in the aetiology of enuresis, but if found on a routine physical examination their removal should again be considered on general grounds.

There remain for consideration two other theoretical causes for enu- *Spina bifida*
resis: spina bifida occulta and allergy. With regard to the former, X-ray *occulta*
examination of the lower part of the spinal column should certainly be
carried out if the hitherto normal child develops intractable incontinence
of urine and possibly also of faeces together with weakness in the lower
limbs at about five years of age. Careful interpretation of the X-ray
findings is always necessary and especially if relatively slight alleged
defects in closure of the spinal canal are used to explain moderate or
minor degrees of enuresis. Allergy has been invoked by Bray and other *Allergy*
workers to explain certain types of enuresis in children; it has been
claimed that treatment based upon this hypothesis has relieved symp-
toms in many persistent cases. It is certainly possible to make, as Bray
has done, a very plausible case for hypersensitivity playing some part
in enuresis; for as with asthma, and its pathogenesis through imbalance
of the nerve-supply to the lungs, so with enuresis there is a balance
between the parasympathetic and sympathetic nerve-supplies of the
bladder muscle and sphincter which might be upset by an allergic
mechanism. Bray's views on this subject have not been generally
accepted, but allergy may well be considered as a possible factor for
persistent enuresis if associated with asthma, hay-fever, eczema, or other
allergic manifestations.

3.–PROGNOSIS

As already indicated, the average case is often most difficult to treat
and may go on for years. Nearly every child with this trouble gets rid
of it eventually and is nearly always better when away from home.
Public schools have seldom any difficulty with this malady in contrast
to preparatory schools where it may prove troublesome.

4.–DIAGNOSIS

Every child with enuresis should be submitted to a full physical examina-
tion to exclude any of the physical factors mentioned above, some of
which may be present, acting as exciting influences rather than as the
underlying cause of the trouble. The urine must be carefully examined, *Examination*
especially for the presence of pus by microscopic investigation. It is *of urine*
useful to know what average quantity is passed in the twenty-four hours.
During this physical examination observations should be made regard-
ing the child's mentality and emotional development. Its confidence
should be gained so that questions directed at eliciting any superficial
causes of friction in the home may perhaps receive helpful answers. The *Psychological*
attitude of mother (and father if present) and nurse to the child should *observations*
be observed and, finally, when the child is not present these adult
members of the household should be catechized in detail as to their

normal attitude to the child in general and to the disorder in particular. The untrained should not attempt any very deep psychological delving, but it is really a matter of common sense to inquire, for example, if the trouble dates from the arrival of a new baby — as it so often does — and to suggest a re-adjustment of household affection which has often superficially become somewhat partisan in favour of the new member. Bed-wetting resulting from fear of getting up in the dark to empty the bladder must be distinguished from enuresis.

5.—TREATMENT

Certain of the lines upon which treatment should be carried out have already been indicated. Intestinal parasites, constipation, phimosis, enlarged tonsils, and adenoids should all receive attention. General hygienic measures should also be instituted to secure fresh air, exercise, a firm mattress, sufficient but not too many bed-clothes, three plain meals a day, a calm well-regulated life with healthy recreation and social activities in which contact with the world and its younger inhabitants is accepted as a matter of course. No moral question should ever arise; bed-wetting is neither 'good' nor 'bad' in this sense and to add 'guilt' to an already emotionally unstable child's troubles can never help. Punishment should not be inflicted, although a tactful system of rewards for the establishment of clean habits is sometimes helpful. Attempts to enlist the child's friendly co-operation by encouraging him to help in tidying up in the morning sometimes provide an incentive to recovery, but again any suggestion of punishment must be scrupulously avoided. All these general adjustments should lead to a calmer home atmosphere but, if enuresis is persistent despite these and other measures to be outlined, or if it is obvious from the start that the child-parental relationships are strained, help should be sought from a trained medical psychologist with special experience in children. Even in these worst cases empirical treatment may eventually prove successful in dealing with the lack of bladder control but the emotional instability may remain to cause other disturbances of a more serious nature.

Treatment for acid urine

If the urine is highly acid more fluid should be taken during the day, especially as weak orangeade, and alkalis may also be given. Apart from this finding, however, which is rare, it is best to restrict somewhat the child's fluid intake and to allow nothing after midday except a small half-cup of milk or water at tea-time.

Treatment of diurnal enuresis

For diurnal trouble the first step is to try to establish some degree of control by making the child pass water, whether necessary or not, at fixed intervals. For a start this may be made at every hour 'as the clock strikes' and the co-operation of the school authorities should be sought to see that this programme is strictly obeyed. After quite a short time this brief interval can generally be managed, the child's confidence increases, and the time for which urine is held can be lengthened. A

jump to two-hourly intervals is generally possible after a week or ten days, and then in another few weeks to three-hourly and four-hourly intervals which, as far as day-time is concerned, is a return to normal. The child with diurnal trouble will be liable even when apparently 'cured' to relapse in moments of fear or other emotion, and such an accident may lead to a temporary return of more persistent trouble, as may also a spell of cold weather.

The nocturnal element in enuresis is more difficult to deal with. The child should be trained to tolerate an increasing amount of urine in the bladder by holding it for longer periods during the day, for this procedure helps to establish some control over the bladder by the higher centres. He should certainly be roused at 10 to 11 p.m.—i.e. at the parents' or nurse's bedtime—and made to pass urine then, but it is probably not wise to disturb the sleep more often than this. *Treatment of nocturnal enuresis*

Restriction of fluids after midday has already been stressed, and the child should not be allowed to go to bed with an over-loaded stomach, although some easily assimilable carbohydrate at bedtime (i.e. a small quantity of glucose) is recommended for promoting a restful sleep. According to the allergic theory kapok bedding should help some children, and it may be worth while to try substituting this for the usual feathers, wool, and hair contents of pillows, mattresses, and eider-downs.

Drug treatment is in many ways the least important part of the therapeutic programme and there are only two measures which are really worth while. First is the use of belladonna which must be given in adequate doses. For a child of six it is possible to begin with 15 minims daily of the tincture in three doses, increasing weekly to 30 minims daily and then to 45 minims daily, or even more. If improvement is effected, and there are no symptoms of excess, the dose can be maintained for a week or so and then gradually decreased. The other drug of value is ephedrine: a $\frac{1}{4}$-grain tablet of ephedrine hydrochloride may be given at bedtime or at the 10 p.m. awakening if bed-wetting always occurs after this. Double this dose may be tried so long as headache and restlessness are not provoked, and it may be combined with the use of belladonna in the day-time. *Drugs*

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EPIDERMOLYSIS BULLOSA

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Reference may also be made to the following title:

PEMPHIGUS

1.–DEFINITION

(Synonym.– Acantholysis bullosa)

421.] Epidermolysis bullosa is a rare condition in which there is a disposition, usually congenital, to form blisters on the skin and in some cases on the mucous membranes, as the result of relatively slight trauma. The cases may be divided into the following types: (1) a simple uncomplicated type; (2) a type in which the predisposition to bullous formation is accompanied by various dystrophies; (3) a type in which analogous clinical signs appear for the first time during adult life.

2.–AETIOLOGY

Heredity In a considerable proportion of cases there is a family history of the disease which may be transmitted by either parent. In exceptional instances adults appear to have acquired the tendency to develop bullae following slight trauma, but in the majority of cases the disposition is

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congenital and is not infrequently associated with various deformities, particularly of the nails. The causation of this abnormal development of the skin is unknown.

3.–MORBID ANATOMY

The vesicles and bullae contain clear or blood-stained serum. The changes which take place in the skin are similar to the changes in pemphigus vulgaris. The bullae are usually situated immediately beneath the corneal layer of the epidermis with negligible changes in the corium, but according to Gans intra-corneal bullae are occasionally met with. In severe cases bullae form between the epidermis and the papillary layer of the corium and are accompanied by oedema and cell infiltration around the vessels. In the latter case resolution is followed by some scarring (see Fig. 8). Engman and Mook demonstrated sections of skin which appeared to show abnormal elastic tissue from non-bullous areas. Small cysts embedded in the skin of the hands and in other areas where bullae have been present are a noticeable feature in some cases. These cysts are said to be derived from the sweat ducts.
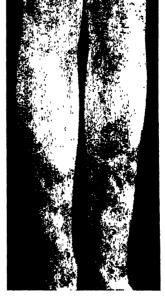
FIG. 8.—Epidermolysis bullosa. Scarring of skin after repeated bullae

4.–CLINICAL PICTURE

Simple type

The chief symptom in the simple type is the formation of bullae on the parts most exposed to injury, namely, the hands, feet, and elbows; but usually no part of the body is exempt from this peculiar reaction; in addition the mucous membranes are involved in about 2 per cent of the cases. This applies particularly to the buccal mucosa. The phenomenon known as Nikolski's sign may be noted in some instances; this is the tendency of the corneal layer of the epidermis to slide and wrinkle after the application of pressure. It is due to lack of cohesion between the horny layer of the skin and the Malpighian layer, but it is not a pathognomonic sign, for it may occur in other bullous diseases. In some instances the bullae have been noted at birth; but in most cases they appear a few days or weeks later. The bullae may be produced easily by artificial trauma, the skin being so vulnerable that pinching it between the fingers is followed by the appearance of a blister within a few hours. The bullae

are flaccid, unilocular, and vary in size according to the situation and type of trauma applied to the skin. Fortunately the patient experiences little discomfort during the development of the bulla, or indeed after it has collapsed, and complete healing takes place with great rapidity. The general well-being of the sufferer is not disturbed by this peculiar maldevelopment 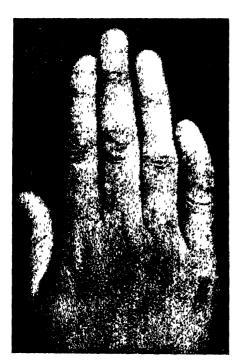of the skin; neither does it influence any intercurrent disease the patient may acquire, but it necessarily limits his occupational and recreative activities.

Dystrophic type

FIG. 9.--Epidermolysis bullosa. Absence of nails, bulla on little finger, and epidermal cysts

In the dystrophic type there is an abnormal development not only of the skin but also of its appendages the nails (see Fig. 9) and not infrequently the teeth. In one of my cases, a girl aged sixteen, the finger-nails were absent from birth, all the teeth had been removed on account of caries, and in addition there was atrophy of the skin from the knees to the ankles. An interesting feature of this case was that the liability to blister was confined to the skin of the limbs. In some cases atrophy involves not only the skin but also the phalanges. In the dystrophic type the mucous membrane of the mouth, conjunctiva, and nose is more commonly affected and may eventually acquire atrophic changes. Hyperidrosis appears to be relatively common in both the simple and dystrophic varieties.

Epidermolysis bullosa acquisita   In the rare cases known as epidermolysis bullosa acquisita the skin appears to react normally for a number of years, then blisters appear following slight trauma. In some this abnormal reaction may disappear spontaneously for some years, only to recur later. The clinical signs are similar to those of the simple type.

5.--COURSE AND PROGNOSIS

In the reported cases there appears to have been some amelioration in later life, for the tendency to blister formation is inclined to diminish and actual recovery has been noted.

6.–DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Given a history of blister formation following slight trauma the diagnosis should not present great difficulty.

In early infancy confusion with pemphigus neonatorum or with congenital syphilis might arise, but the contents of the bullae in epidermolysis bullosa are clear, whereas in the other complaints the fluid is opaque. In long-standing cases atrophy of the skin and deformity of the nails will usually be found. *Diagnosis from pemphigus neonatorum and syphilis*

In pemphigus vulgaris the bullae arise independently of trauma and are more distended than in this disease. Further, grave constitutional disturbances appear when pemphigus is established, and it is doubtful if pemphigus ever occurs in young children. *From pemphigus vulgaris*

7.–TREATMENT

As the malady is due to a developmental defect it is unlikely that any satisfactory remedy can be found, and the treatment therefore is palliative. Beinhauer, however, reported improvement of the general health and cessation of the bullous lesions in a case of the acquired type following the injection of a purified extract of the anterior-pituitary-like hormone of pregnancy urine three times weekly for one month. Kittredge, in an acquired case of twenty years' duration, claimed to have obtained a successful result from the administration of iron cacodylate, a blood-coagulating preparation, calcium, and X-ray therapy. The iron cacodylate was given intramuscularly at one- to three-day intervals for about six weeks, in doses increasing from $\frac{1}{2}$ grain at the beginning of the treatment to a maximum of 2 grains.

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EPIDIDYMITIS

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Reference may also be made to the following titles:

COLIFORM BACILLUS INFECTION   SYPHILIS

GONORRHOEA   TUBERCULOSIS

422.] Epididymitis can most conveniently be discussed under two main headings depending on the mode of onset, whether acute or chronic.

1.–ACUTE EPIDIDYMITIS

Causes In over 90 per cent of cases acute epididymitis is due to gonococcal infection. In the great majority of the remainder *B. coli* is responsible, and a small proportion are due to staphylococci or other pyogenic

organisms. Very exceptionally tuberculous epididymitis begins as an acute condition, but in the overwhelming majority of cases it is chronic from the outset. In some cases the epididymis is acutely inflamed as a result of injury or such infectious diseases as mumps, influenza, or enteric fever, but usually then the condition is overshadowed by an associated orchitis.

(1)—Gonococcal Epididymitis

(a) Aetiology

Gonococcal epididymitis is one of the most frequent complications *Incidence* of gonorrhoea in the male, occurring usually after the second week. Estimates of its incidence by different authors vary greatly; some put it as high as 30 per cent, but in two military hospitals which I knew in the Great War the percentage in cases that were free of the complication on admission was less than two. The figure depends very greatly on the circumstances in which the patient is treated and the skill of the medical attendant, as will be understood from what follows; but in ordinary civilian treatment centres in this country the percentage incidence after first attendance is probably between five and eight.

How the infecting organisms reach the epididymis in an acute *Path of* epididymitis of bacterial origin is not definitely known. Some think that *infection* in a small percentage the infection is haematogenous, more believe that the route is by the lymphatics, but the great majority consider that it is more direct, along the canal of the vas deferens. This presupposes infection of the posterior urethra, and most workers would agree that there is usually also an infection of one or both seminal vesicles. Transference of the infection by spread of the inflammatory process along the vas does not explain those cases in which epididymitis rapidly follows (within 24 hours) such an intervention as passage of an instrument along the urethra, or prostatic and vesicular massage, and the general belief is that in most cases the epididymis is infected by secretion carried mechanically to the tail of the epididymis. Opinions differ as to the mechanism by which the infective matter is conveyed against the stream of the vas, and it is necessary here only to mention without elaborate discussion the chief methods that have been suggested by different authors. They are: (1) by urine forced from a full bladder through an ejaculatory duct into the seminal vesicles and thence by overflow into the vas (Pelouze); (2) by pressure on an infected seminal vesicle and regurgitation of the secretion along the vas; (3) by peristalsis of the vas against a blocked ejaculatory duct; (4) by reverse peristalsis of the vas (Oppenheim and Löw).

Though opinions differ as to the mechanism by which the infection *Provocative* is carried to the epididymis, there is very close agreement about the *factors* procedures which provoke gonococcal epididymitis. They are such errors of treatment as irrigation of the urethra at too great a pressure, the use in local treatment of chemicals that are too strong, the passage of instruments, massage of the prostate and vesicles during the acute

and subacute stages, and such errors on the patient's part as indulgence in violent exercise, sexual intercourse, perhaps allowing the bladder to become too full, and perhaps also allowing the bowels to become constipated, since passage of a hard stool over an infected seminal vesicle and prostate must have the same effect as massage of the prostate and the seminal vesicles. Most of these causes seem to be either such as produce undue irritation and swelling of the posterior urethra, which would be expected to block the ejaculatory ducts, or such as apply pressure to the seminal vesicles, ampullae of the vas deferens, and ejaculatory ducts; and they favour the hypothesis that epididymitis occurs when an infected vesicle is pressed upon, by massage or other cause, and the secretion cannot escape freely into the urethra.

(b) Morbid Anatomy

Histological studies show that when the infection reaches the tail of the epididymis it passes into the peritubular tissues, setting up acute inflammation there, with perhaps the formation of small abscesses, though clinical abscess is rare in gonococcal epididymitis. The inflammatory process spreads rapidly for a variable distance in the direction of the globus major. The tunica vaginalis is often inflamed, causing an inflammatory hydrocele. The eventual result is more or less fibrosis and compression of the tube of the epididymis, with consequent occlusion in over 75 per cent of cases.

(c) Clinical Picture

Pain

Usually following closely (within 24 hours) on one of the errors in treatment or the patient's conduct mentioned above, the patient has a sharp pain within the scrotum, or this may follow some hours after the onset of pain in the groin on the affected side owing to a preliminary vasitis. In some of these cases when the right side is affected there may be severe pain in the right iliac fossa, and this, with the vomiting and rise of temperature which occur at the same time, may lead to an erroneous diagnosis of appendicitis. When the epididymis becomes inflamed the patient complains that the testicle on the affected side has become very tender and so painful that he can walk only with difficulty, and he may vomit on the least jar.

Imitating appendicitis

Examination of patient

On examination the testicle is practically unaffected, but the epididymis behind it is felt to be greatly enlarged, like a small bolster applied to the back of the testicle. There is often acute tenderness and some diffuse swelling of the cord. Even when, as frequently happens, there is an inflammatory hydrocele it is usually easy to detect the enlargement and inflammation of the epididymis at the back of the distended scrotum, the skin of which is usually reddened and oedematous.

Urethral discharge

Commonly the urethral discharge ceases at the onset of this complication; or the cessation may occur some hours previously; sudden cessation of discharge in acute gonorrhoea is ominous, as it often heralds a complication such as prostatic abscess or epididymitis.

Constitutional symptoms commonly occur in the form of a rigor *Constitutional* followed by a high temperature and in some cases by vomiting. Some- *symptoms* times the pain is so severe as to require morphine, and often in these cases the swelling of the epididymis is comparatively small but the organ is very hard. In other cases signs and symptoms are comparatively slight, with inflammation practically restricted to the tail and middle of the epididymis. In these cases constitutional and local disturbance may be so slight that the patient can go about his work if his testicle is well supported.

Symptoms usually begin to abate in a few days, except in the rare event of suppuration, which is indicated by increase of local and constitu-tional symptoms, rigors, fever, and sweats, and eventually fluctuation with evacuation of an abscess. In the average case, on subsidence of all symptoms a hard nodule is left in the globus minor and sometimes another can be felt in the middle of the epididymis; such nodules may persist for years.

(2)—Acute Epididymitis due to *B. coli* and Other Organisms

Acute epididymitis due to *B. coli* pursues much the same course as the gonococcal, and the diagnosis is made only by bacteriological tests. When the inflammation is due to staphylococci or other pyogenic organisms after such operative measures as removal of the prostate or litholapaxy, suppuration appears to occur more frequently.

(3)—Acute Tuberculous Epididymitis

Acute tuberculous epididymitis is so similar in onset to acute epididym-itis due to other causes that its true nature may not be discovered until later, when it passes on to the formation of a sinus and develops the characteristics of the far commoner chronic tuberculous epididymitis.

(4)—Recurrent Epididymitis

Some patients who have at one time or another suffered from urethritis, perhaps with acute epididymitis, may be troubled by repeated attacks of pain in the cord, often followed by pain and swelling of the epididymis. Although in some of these cases, diagnosed as recurrent epididymitis, *Causes* the cause may be a recrudescence of bacterial activity in the parts affected, in the great majority which I have seen the condition was clearly due to inability of the seminal vesicles to empty their contents freely into the urethra. The signs do not suggest active inflammation but obstruction and distension, and the pain and swelling are usually relieved by prostatic massage, provided that this produces a flow of prostatic and vesicular fluid into the urethra. It is true that occasionally *Part played* prostatic massage may aggravate the condition, but this may be due to *by obstruction* its failure to clear the obstruction. The view that obstruction probably causes most cases of recurrent epididymitis is supported by the experience of H. Boeminghaus, who says that in a number of cases in elderly men

in whom sexual intercourse has become attended by severe pain in the cord and often followed by swelling of the epididymis, permanent relief has been afforded by a vasostomy on the affected side.

(5)—Diagnosis

As a rule there is not any difficulty in the detection of enlargement of the epididymis in the absence of coincident orchitis. Even when there is an inflammatory hydrocele obscuring the front of the scrotum, it is generally quite easy to make out the hard, painful, enlarged epididymis at the back of the scrotum. If a hydrocele is not present or when it has been tapped, the bolster-like acutely tender epididymis, enlarged especially at its lower end, contrasts very strongly with the corresponding organ on the other side. The case in which the epididymitis is secondary to and overshadowed by orchitis belongs properly to that section and will not be considered here. In some very acute cases the pain may appear to be localized chiefly in the lower abdomen and, with the vomiting which commonly occurs in such cases, an abdominal tragedy may be feared. This occurs most frequently when, in the course *From appendicitis* of an attack of gonorrhoea, before the epididymis has become enlarged the patient suddenly has symptoms rather closely simulating appendicitis. Probably many appendices have been removed on suspicion in such cases, and the error might be prevented if the possibility that the symptoms are really due to acute vasitis were remembered. In such a case palpation of the cord causes pain, and probably rectal examination would disclose a tender and swollen seminal vesicle. The cause of the swelling is not difficult to trace if certain pitfalls are avoided.

Diagnosis of gonococcal infection An acute epididymitis that is not obviously due to injury or a sequel of such an operation as prostatectomy or litholapaxy is so very commonly due to gonococcal infection that cases in which the cause is some other infection, torsion of the cord, or obstruction to the flow of semen into the urethra, are apt automatically to be diagnosed as gonorrhoeal. It follows that a diagnosis should never be made until the urine and any urethral secretions have been bacteriologically examined. When the cause is gonococcal there is usually no difficulty in making a certain diagnosis even if the patient denies any preceding urethral discharge.

Of B. coli infections *B. coli* infections are also easy to diagnose, as the urine commonly swarms with these organisms so much as to be hazy, and a loopful of it cultivated on an agar slope shows a very strong film of growth in less *Of other infections* than twelve hours. An acute epididymitis due to other pyogenic organisms might cause difficulties so that the diagnosis would be made only by exclusion of the more common causes and perhaps by the formation of an abscess and the discovery of the causal organism in the contents.

Of tuberculous infection In acute tuberculous epididymitis the cause may not be discovered at first, unless it is perfectly obvious that the patient is not suffering from gonorrhoea and certainly has tuberculous lesions elsewhere. In this case a bacteriological examination of the centrifugalized deposit of the urine may quickly reveal tubercle bacilli. Failing an early diagnosis the nature

of the infection becomes clear at a later stage when the epididymis becomes nodular and the vas thickened and beaded and fistulae form in the manner typical of tuberculous epididymitis. Epididymitis following a blow may be attributed entirely to the injury, when this might be only the precipitating agent. Accordingly in such cases it is wise to examine for bacterial infection.

Sudden onset of pain in the testicle and perhaps sudden relief *Of torsion* without any history or sign of infection would suggest torsion of the *of cord and obstruction* cord. In the same category are those cases of so-called recurrent epididymitis discussed above, in which owing to previous inflammation of the posterior urethra and the prostate one or both ejaculatory ducts have become more or less obstructed. In such cases, although the pain may be acute, there is little or no evidence of active inflammation either in local signs or in constitutional disturbance.

(6)—Treatment

Prevention of epididymitis is very important, especially in gonorrhoea *Prevention* affecting young persons, because the affected epididymis is so frequently blocked, and double epididymitis is followed in a very high proportion of cases by azoospermia and sterility. In acute gonorrhoea any irrigation should be at very low pressure, local applications should be mild, instruments should not be passed (unless necessary in retention of urine), the prostate and seminal vesicles should not be massaged, and exercise should be of the mildest character until the urethritis has subsided. Avoidance of sexual excitement and of food, drink, or medicine likely to increase the urethral irritation is important, and the bowels should be regulated to prevent pressure of hard scybala on the seminal vesicles and prostate. I believe also that atropine or belladonna, as originally advised by C. Schindler, is a useful preventive of epididymitis. Schindler's recommendation is based on animal experiments in which reverse waves along the exposed lower end of the vas and ejaculatory ducts, provoked by irritating the posterior urethra, were prevented by putting the nerves supplying the parts under the influence of atropine. As a routine I include belladonna in the medicine prescribed for an ordinary case of gonorrhoea in the male, and if signs of acute posterior urethritis appear a suppository containing atropine sulphate $\frac{1}{70}$ grain or dry extract of belladonna $\frac{1}{4}$ grain is prescribed for use each night and morning. In cases of urethral infection with other organisms irrigation of the urethra with a suitable antiseptic lotion before and after the passage of any instrument through the posterior urethra, apart from other advantages it has, seems likely to prevent some epididymitis, and a preliminary vasectomy is often practised as a preventive of the epididymitis that is apt to follow prostatectomy.

In treatment the following measures are usually applicable to all cases of acute epididymitis except perhaps the tuberculous, which will be discussed under chronic epididymitis. Rest is very important. If the inflammation is not very acute, a well-fitting suspensory bandage may

Suspensory bandage

give enough support to allow the patient to get about. The scrotum and contents must be well elevated towards the pubes on a pad of cotton wool and held so firmly that they are not easily jarred. Many ingenious methods of achieving this have been published, probably the simplest being a tightly fitting jock-strap as worn by athletes. A well fitting suspensory bandage of the Horand pattern serves very well, but the ordinary little net bag commonly sold to the general public as a suspensory bandage is by no means so useful. Pelouze recommended a double spica of six-inch-wide muslin tightly applied, with the scrotum and contents, previously covered with cotton wool, pulled well forward and upward. Such supports if well applied are often sufficient to enable the patient to go about his work, but in more severe cases rest in bed is

Diathermy

indicated. Heat is valuable; it can be applied either by poultices over glycerin of belladonna or better by diathermy, and in this the better results seem to follow the application of the electrodes to the testicles and the prostate than when the non-testicular electrode is placed elsewhere, as on the abdomen or under the buttocks. Diathermy seems also to be the best method of promoting resolution of the nodule so commonly found in the tail of the epididymis long after subsidence of the attack.

Surgical measures

In very acute cases many, chiefly American, authors recommend surgical exposure of the epididymis and puncture with a tenotome or cataract knife of the parts that are especially tense, any wound which gives exit to pus being enlarged with a probe. The operation is said to give very rapid relief, and it seems possible that in some cases it may prevent obstruction of the tube of the epididymis. For technical details special works should be consulted.

Drugs

Of general measures numerous remedies have been recommended for intravenous injection, including 5 to 10 c.c. of 10 per cent calcium chloride or gluconate solution (preferably the latter) given very slowly every day for four or five days; 0·15 gram to 0·3 gram of a sulpharsphenamine preparation given every other day; and 0·01 gram of mercury cyanide dissolved in 10 c.c. or more of 0·9 per cent saline daily.

Treatment of recurrent epididymitis

For those cases of recurrent epididymitis which are probably due to interference with the emptying of the seminal vesicles into the urethra, prostatic and vesicular massage, with diathermy to the prostate and appropriate treatment of the urethra if there is evidence of chronic posterior urethritis, usually suffice. If these measures fail, it is necessary to consider washing out the seminal vesicle through the vas with colloidal silver, or vasostomy, as recommended by Boeminghaus.

2.—CHRONIC EPIDIDYMITIS

423.] As already stated epididymitis that is chronic from the beginning is due to tuberculosis in probably more than 90 per cent of cases.

The other chief causes of chronic enlargement of the epididymis are a previous acute inflammation, syphilis, infection with organisms of low pathogenicity, new growths, and cysts.

(1)—Tuberculous Epididymitis

Authorities are divided about the manner in which the epididymis *Source of* first becomes infected in tuberculous epididymitis, some maintaining *infection* that it is haematogenous and others that the route is from the prostate and vesicles and along the vas, either in the lumen or by the lymphatics. In some cases the infection is said to have travelled from the urethral meatus. From the fact that in a high proportion of cases the prostate and vesicles are obviously affected and sooner or later the other epididymis, and that in almost all cases the disease starts in the epididymis, it seems to follow that in the great majority of cases the disease spreads to the epididymis from the prostate and vesicles. On the other hand tubercle bacilli are said to have been found in the healthy testicle and epididymis, and it is reasonable to suppose that, without pre-existing foci in the bladder, prostate, and vesicles, lowering of the local resistance by trauma or bacterial (e.g. coliform or gonococcal) infection might lead to a primary tuberculous epididymitis. It may be that the epididymis is essentially more susceptible than the testicle.

The onset may be acute, but in most cases it is insidious, with mild *Clinical* symptoms in the form of a dull ache which leads to an examination *picture* and the discovery of one or more nodules in the epididymis, usually in the globus minor or major. In more advanced cases the whole epididymis is enlarged and nodular. The process sometimes becomes arrested temporarily, but in most cases suppuration, adhesion to the scrotum, and the formation of fistulae occur comparatively early. A chronic hydrocele often forms and may interfere with examination. The cord, especially the portion within the scrotum, is also thickened and usually beaded. Sooner or later, unless arrest is effected, the process spreads to and destroys the testicle. In a large proportion of cases there are symptoms of urethritis, and nodules can be detected in the prostate and vesicles.

The first granuloma usually appears in either the globus major or *Morbid* minor. It enlarges and caseates in the manner of tuberculous lesions *anatomy* and may spread as one caseating mass throughout the epididymis, or a number of nodules may be formed. Sooner or later similar granulomas usually appear in the body of the testicle, the tunics are infiltrated, and the organ becomes adherent to the skin, through which fistulae then communicate with the broken-down tuberculous nodules and cavities in the epididymis and possibly testis. Instead of the process going on to the formation of fistulae it may become arrested with eventual fibrosis of the lesions. Tuberculous nodules often form in the vas (usually at both ends rather than in the middle) and, as mentioned above, in the prostate and vesicles. Histologically the appearances are those of tuberculous lesions elsewhere.

Clinical picture

The disease usually affects adolescents and young adults but older and younger subjects are not immune.

Diagnosis

The diagnosis in a typical case is easy. It may be necessary to tap the hydrocele to enable one to appreciate the nodular character of the epididymis. This, with the quiescence of the symptoms, the early and multiple fistulation, the nodular thickening of the cord in the scrotum, and the presence of the tuberculous foci elsewhere, including the prostate and seminal vesicles, should lead to an examination of the deposit of the centrifugalized urine and of the discharge from the fistulae for tubercle bacilli.

From chronic obstruction

Aching and mild swelling of the epididymis due to chronic obstruction to the outflow of semen into the urethra might be so chronic as to arouse a suspicion of tuberculous epididymitis, but the swelling is smooth, the condition is not usually progressive, and usually the constitution of the patient and the absence of other signs of tuberculosis should make its exclusion easy.

(2)—Chronic Non-Tuberculous Epididymitis

A chronic non-tuberculous epididymitis not apparently due to tuberculosis or a consequence of urethritis may be due to a haematogenous infection with organisms of mild virulence. It is diagnosed by exclusion.

(3)—Syphilis

Syphilis affecting the epididymis exclusively is rare. Cases have been described in which a nodule formed in the globus major during the so-called secondary stage, and a chronic gummatous epididymitis has been described, but commonly any syphilitic infection of the epididymis is part of and overshadowed by orchitis. The quietness of a syphilitic epididymitis with the rarity of its occurrence might raise a suspicion that it was tuberculous, but the history and associated signs would probably prevent any error.

(4)—New Growths and Cysts

New growths within the scrotum are unlikely to be mistaken for any form of epididymitis as commonly they first affect the testicle. Cysts of the epididymis should cause no difficulty in diagnosis.

(5)—Treatment

The forms of chronic epididymitis to be considered here are tuberculous and the chronic non-tuberculous, whether following acute epididymitis or chronic from the first and not associated with urethritis.

Of tuberculous epididymitis

The treatment of tuberculous epididymitis is that appropriate for tuberculosis generally and, if circumstances permit, surgical removal of the diseased epididymis or both testicles and epididymis according to the stage the disease has reached.

For the chronic non-tuberculous epididymitis it may, if palliative *Of non-*
measures fail, be necessary to consider epididymectomy or epididym- *tuberculous*
otomy. *epididymitis*

The treatment of syphilitic epididymitis is naturally that of the disease *Of syphilis*
generally, no local measures being usually required.

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EPILEPSY

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Reference may also be made to the following titles:

1.–DEFINITION

424.] The term epilepsy is used in somewhat different senses by different *Nature of epilepsy* writers. In order to define it satisfactorily it is necessary to consider both symptomatology and aetiology. Epilepsy is a paroxysmal and transitory disturbance of the functions of the brain developing suddenly, ceasing spontaneously, and showing a marked tendency to recurrence. In its most typical form it is characterized by the sudden onset of loss of consciousness followed by tonic spasms and clonic contractions of the muscles, which cease spontaneously after about half a minute and leave the patient in a state of unconsciousness from which he gradually recovers. There are, however, many varieties of epileptic attacks, the character of which depends upon the site of origin and the extent of the cerebral disturbance. For example, impairment or loss of consciousness may occur without movement as in *petit mal*, or movement may occur without loss of consciousness as in the milder forms of Jacksonian attack; or the predominant feature of the attack may be an abnormal mental state or a sensory hallucination. Thus the content of the epileptic attack is variable and no single feature, not even loss of consciousness, is invariably present. The sudden onset, rapid development, spontaneous cessation, and tendency to recurrence of the attack, together with its cerebral 'signature', are the constant and definitive features.

Thus defined, epilepsy is a symptom of a large number of disorders, *Nature of associated disorders* including congenital abnormalities of the brain, inflammatory states of the nervous system, such as syphilis, intracranial tumour, head injury, cerebral arteriosclerosis, and many abnormal metabolic states, to mention only a few. Such causes, however, can be found in only a minority of patients suffering from epilepsy. Most epileptics do not show any physical or metabolic abnormality. Epilepsy in persons who appear to be otherwise normal is usually described as 'idiopathic epilepsy'. Some writers, to indicate the multiplicity both of the forms of epilepsy and of its causes, speak of 'the epilepsies', and regard idio- *The epilepsies* pathic epilepsy as comprising a heterogeneous group of patients united only by our ignorance of the cause of their attacks. Others consider that a tendency to epilepsy, not uncommonly inherited, underlies the disorder in many cases in which a local lesion of the brain acts as an immediate or precipitating cause, and so justify the unitary character of the conception of idiopathic epilepsy. The truth appears to be that in some individuals there is a predisposition to epilepsy, sometimes inherited, which is strong enough to manifest itself in the absence of any local lesion of the brain. Others again only become epileptic when a local lesion is added to a pre-existing disposition. In a third group the local lesion, or an abnormal metabolic state, or, in an extreme case, a convulsant toxin is capable of causing epilepsy in the absence of any predisposition. Confusion as to the meaning of epilepsy has arisen from the use of this term to describe both a symptom common to a number

of disorders and a predisposition to convulsions assumed to underlie the symptom in certain cases, and doubt as to the validity of the conception of idiopathic epilepsy is suggested when a patient previously thus labelled proves in time to have had a latent local cerebral lesion which is considered to be an adequate cause of the attacks. In the present state of our ignorance the classification of the epilepsies must be mainly pragmatic, and there is a practical justification for the distinction between idiopathic and symptomatic epilepsy so long as the provisional character of the distinction is borne in mind.

2.—AETIOLOGY

425.] It is clear from what has been said that the aetiology of epilepsy, like that of many disorders, is complex, and that in a single patient several factors may combine to cause the attacks. In considering aetiology it is most convenient to begin with the disturbance of cerebral function which underlies the attack, then to discuss proximate causes, such as local lesions of the brain, and to pass from these to more remote causes, such as abnormal metabolic states, inherited predisposition, age, and sex.

(1)—The Physiological Disturbance

The nature of the disturbance of function of the cerebral neurones which is expressed as an epileptic attack is still unknown. Physiologically there is an explosion of energy leading to incoordinate discharge which may spread rapidly and widely as in a major attack, or more slowly and locally as in a Jacksonian attack. Presumably its immediate antecedent is an altered physico-chemical state of the nerve-cells. It is probable that the recent study of changes of electrical potential of the cortical neurones will throw some light on its nature. There is evidence, however, that numerous and varied factors influence the liability to the epileptic discharge. As Lennox puts it in an illuminating metaphor, the epileptic is like a reservoir the level of which is controlled by a dam. Many factors may either raise the level of the water or lower that of the dam and so cause an overflow which manifests itself in a convulsion.

(2)—Lesions of the Brain

Congenital abnormalities Many types of cerebral lesion may cause epilepsy or at least act as 'triggers' in releasing the attacks. Congenital abnormalities include porencephaly and atrophic lobar sclerosis, which is the pathological basis of congenital cerebral diplegia. Tuberous sclerosis is a rare disorder of development in which epilepsy is associated with mental deficiency and adenoma sebaceum (see EPILOIA, p. 117). Epilepsy occurs in over 50 per cent of cases of infantile hemiplegia, which in its congenital form is often due to birth injury. An acute cerebral lesion in childhood causes convulsions and hemiplegia and may leave the child epileptic. This has

been attributed to acute encephalitis (the Strumpell-Leichtenstern *Acute* form), acute polio-encephalitis, and to a vascular lesion within the dis- *encephalitis* tribution of the middle cerebral artery. Convulsions may occur as a symptom of other forms of acute encephalitis and less often of cerebral abscess and acute meningitis, and are also seen in the rare degenerative cerebral disorders of childhood, such as amaurotic family idiocy and cerebral diffuse sclerosis.

In adult life syphilis sometimes causes epilepsy, which is commoner *Syphilis and* in dementia paralytica than in meningo-vascular syphilis. Disseminated *disseminated* sclerosis is a rare cause. *sclerosis*

Twenty or thirty per cent of patients with an intracranial tumour have *Intracranial* convulsions which sometimes precede other symptoms and signs of the *tumour* tumour by several years. Parasitic cysts in the brain are sometimes a cause of epilepsy. Cerebral cysticercosis is by no means rare in soldiers who have served in India (see CYSTICERCOSIS, Vol. III, p. 523). Hydatid infection most often occurs in Australia (see HYDATID DISEASE).

(3)—Head Injury

The importance of trauma in the aetiology of epilepsy is difficult to *Traumatic* assess. Figures ranging from 4·5 to 25 per cent have been given by different *epilepsy* authors as the proportion of patients developing epilepsy after gunshot wounds of the head during the Great War. Wagstaffe found that the incidence of epilepsy was much higher after an injury which penetrated the dura than after slighter injuries, and Foerster and Penfield demon- strated that after such injuries the brain might be united to the dura by a vascularized scar. It is probable that after head injuries in civil life not more than 5 to 10 per cent of patients develop epilepsy. The latent interval between the injury and the onset of convulsions is usually less than two years but may be considerably longer.

When a head injury sufficiently severe to cause concussion is followed by epilepsy a causal relationship may be presumed. Equal importance cannot be attached to a history of slighter injuries such as is fairly commonly given by epileptics. If a slight head injury precipitates epilepsy there is probably a predisposition to it.

(4)—The Cerebral Circulation

For many years spasm of the cerebral arterioles was regarded as the disturbance of function immediately preceding an attack. The researches of Lennox and his collaborators, however, have shown that there is no evidence that any functional disturbance of the cerebral circulation precedes an attack of idiopathic epilepsy. Nevertheless, cerebral ischaemia if sufficiently severe may cause convulsions, as is seen when the circula- *Stokes-* tion is temporarily interrupted by heart-block in the Stokes-Adams *Adams* syndrome. *syndrome*

Convulsions are a prominent symptom of the hypertensive encephalo- *Hypertensive* pathies, such as occur in association with a raised blood-pressure in *encephalo-* acute nephritis, malignant hypertension, eclampsia, and acute lead *pathy*

poisoning, and, though toxic factors may also be present in such case, it is probable that the main cause of the convulsions is cerebral ischaemia. Focal cerebral vascular lesions may be ushered in by convulsions, and this is commoner in cerebral embolism than in thrombosis or haemorrhage. In late middle life and old age the commonest cause of epilepsy is cerebral arteriosclerosis.

(5)—Metabolic Factors

Epilepsy may occur as a symptom of various abnormal metabolic states. Anoxaemia may precipitate attacks in sufferers from idiopathic epilepsy, and so also may hyperventilation induced by over breathing. Generalized convulsions sometimes occur in tetany due to either a *Hypo-* lowered blood calcium or to alkalosis. Hypoglycaemia resulting from an *glycaemia* overdose of insulin may cause a seizure, and epilepsy may be a prominent symptom of persistent hypoglycaemia caused by a tumour of the pancreatic islet cells of Langerhans, but there is not any convincing evidence that hypoglycaemia plays a part in the aetiology of idiopathic epilepsy.

The part played by water metabolism in the causation of epilepsy is still obscure, but there is some evidence that in epileptics attacks may be induced by water retention. In spite of these facts innumerable attempts to discover some constant metabolic abnormality underlying idiopathic epilepsy have failed, nor is there any evidence that endocrine abnormalities play any part in its aetiology, though certain dysplasias of endocrine origin are fairly common in epileptics (see p. 108) and menstruation is well known as a precipitant of the attacks in women.

(6)—Allergy and Migraine

Allergy plays no large part in the aetiology of epilepsy. Both in experimental animals and in man convulsions may occur as a result of anaphylactic shock, and sensitiveness to a specific food substance *Epilepsy and* sometimes causes epilepsy. Occasionally epilepsy is associated with *asthma* asthma or some other allergic state in the same individual, or in different *Migraine* members of the same family. Both migraine and epilepsy are common disorders, and it is doubtful if their association either in the same individual or in the same family occurs more often than would be expected *Migrane-* on a chance basis. In rare instances a sufferer from migraine has some *epilepsy* migrainous attacks which terminate in a convulsion, a condition known as migraine-epilepsy.

(7)—Convulsant Toxins

Many substances possess the property of exciting convulsions. Some, such as thujone (the convulsant principle of absinthe), camphor, cocaine, and picrotoxin, appear to act directly upon the nerve-cells. Others, such as ergot, lead, and carbon monoxide, and the endogenous toxins of uraemia and eclampsia, probably act indirectly. Others again, such as nitrous oxide, alcohol, ether, chloroform, and the organic arsenicals,

cause convulsions only rarely and in special circumstances. Strychnine and tetanus toxin act mainly upon the brain-stem and spinal cord. The immature nervous system of the child may react by a convulsion to any acute infection. Idiopathic epilepsy has been attributed to a hypothetical convulsant toxin, but this has never been proved to exist.

(8)—Deficiency Disorders

Rickets is the only common deficiency disorder of which convulsions *Rickets* are an important symptom. Epilepsy may occur also in pellagra, which *Pellagra* is believed to be due to dietary deficiency; and there is evidence that lack of vitamin A may render the organism sensitive to ergot.

(9)—Heredity and Predisposition

Attempts have been made to minimize the importance of heredity in *Familial* the aetiology of epilepsy, but the facts speak for themselves. In a series *incidence* of 200 epileptics of the hospital class, 56, or 28 per cent, knew of relatives similarly affected, compared with 10 per cent in a control group of patients suffering from nervous disorders other than epilepsy. Lennox found the incidence of seizures among near relatives of epileptics to be six times that of a control group. Even among the near relatives of sufferers from symptomatic epilepsy, i.e. those in whom epilepsy followed an injury to the brain, the incidence of seizures was nearly three times as high as in the control group. This is strong evidence in favour of the view that a proportion of persons who develop epilepsy after a brain injury already possess an inherited predisposition to the disorder. Among affected members of the family the relationship of parent and child occurs in about a quarter of the cases, that between uncle or aunt and nephew or niece in a quarter, that between siblings in a quarter, and a more remote relationship in the remainder. The risk of an epileptic parent transmitting the disorder to his or her child is not very great and may be roughly estimated at 1 in 10. The risk is greater when there is already a family history of the disorder than when this is absent.

Since what is inherited is a tendency to epilepsy which may remain latent, there is at present no means of discovering how many members of an affected family inherit the tendency but do not manifest the disorder. Since Mendelian laws are concerned with the numerical proportions in which transmitted characters are inherited by the offspring, it is clear that there are not available the data from which to draw conclusions as to the mode of inheritance of epilepsy. Save in exceptional cases there is no hereditary relationship between epilepsy and insanity or any other disorder.

(10)—Epilepsy and Infantile Convulsions

Patrick and Levy found that infantile convulsions occurred at least five times as frequently in epileptics as in normal children, and that among non-epileptic children who had early convulsions a family history

of both infantile convulsions and epilepsy was commoner than in a control group. In my series of epileptics, infantile convulsions occurred in 28 per cent and were nearly twice as common in those with a family history of the disorder than in those with none. In some normal children therefore the occurrence of infantile convulsions may denote an inherited tendency to epilepsy and serve as a warning which may be of prophylactic value.

(11)—Sex and Age

Sex incidence   Females suffer from epilepsy slightly more frequently than males. The ratio of females to males in Gowers' series of 3,000 cases was 13 to 12.

Age incidence   In three-quarters of all cases idiopathic epilepsy begins before the age of twenty, in almost half the cases during the second decade. In only 10 per cent is the onset after the age of thirty. During the first twenty years of life there is an increased liability to the onset of convulsions at certain ages, namely, during the first three years of life, at the age of seven at the time of the second dentition, and during the years following puberty.

Epilepsy as a symptom of intracranial tumour and cerebral syphilis is commonest between the ages of forty and sixty, and after sixty is usually due to cerebral arteriosclerosis.

(12)—Psychological Factors

A few psychoanalysts have interpreted the epileptic fit as a psychological symptom, but it is in only a small minority of cases that there is any reason to think that psychological stress plays any part in causation, though fear or excitement may act as precipitants of an attack.

3.—MORBID ANATOMY

426.] In a sense there is no morbid anatomy of epilepsy, since epilepsy is a disorder of function common to many pathological states and may also occur in the absence of any discoverable lesion of the brain. If all cases of symptomatic epilepsy are excluded, most epileptics possess a brain which appears to be normal. A minority, however, exhibit minor abnormalities, such as localized leptomeningeal thickening, excess of fluid in the subarachnoid space, asymmetry or dilatation of the ventricles, and scarring or atrophy of part of the brain. The most constant microscopical changes are focal lesions in Ammon's horn, which when recent consist of foci of tissue destruction which are later followed by gliosis. Some of these abnormalities may well be the results of the convulsions; others are the sequelae of traumatic or inflammatory lesions and may act as irritant foci which precipitate attacks.

4.–CLINICAL TYPES

(1)—Major Epilepsy (*Grand Mal*)

427.] Of the many types of epileptic attack major epilepsy is both the commonest and the most dramatic. The following is a description of a typical major attack.

Pre-convulsive symptoms Epileptic patients frequently exhibit symptoms for some hours or even for a day or two before an attack. Mental changes, such as irritability and depression, abnormal feelings referred to the head, giddiness, and muscular twitches, are the commonest of these pre-convulsive symptoms.

Aura About 60 per cent of epileptics experience an aura or warning of the attack. It is a focal symptom due to the beginning of the cortical epileptic discharge and perceived by the patient before consciousness is lost. Since the attack may begin at a number of different sites in the brain there is a corresponding diversity of auras. The aura may consist of a psychical state such as a feeling as if everything that is being experienced has happened before, or may originate within the sphere of the special senses, consisting, for example, of an olfactory or a gustatory hallucination, a complex visual scene or a flash of light, or the hallucination of hearing a phrase or word uttered or a loud sound. Somatic sensibility may provide the aura in the shape of a sensation of numbness, tingling, or electric shock referred to part of the body. Occasionally such a sensory aura is painful. A diffuse disturbance of somatic sensibility, such as a feeling of being disembodied, may occur, and peculiar indescribable visceral sensations usually referred to the abdomen constitute a common form of aura. There are many forms of motor aura, of which the commonest is a brief spasm or clonic movement such as rotation of the head to one side or flexion of one upper limb, of which the patient is aware for a second or two before he loses consciousness. Vertigo is a common aura, especially in minor epilepsy.

Convulsion The convulsion may begin with a loud cry, but this is more often absent than present. Consciousness is lost either at the very beginning of the attack or else immediately after the aura, and if the patient is standing he falls to the ground often with sufficient violence to injure himself. Scars on the face from this cause are therefore common in epilepsy. *Tonic phase* The first phase of the convulsion proper is a tonic spasm of the muscles, hence known as the 'tonic phase'. This is usually symmetrical on the two sides of the body, but it is not uncommon for the head and eyes to be rotated to one side and for the mouth to be drawn to one side by asymmetry in the degree of facial spasm. The upper limbs are usually adducted at the shoulders and flexed at the elbows and wrists. The fingers are flexed at the metacarpo-phalangeal and extended at the interphalangeal joints, the thumb being adducted. The lower limbs are usually extended, with the feet inverted. Owing to spasm of the muscles of respiration breathing is temporarily arrested and the patient becomes increasingly cyanosed. The tonic phase lasts

Clonic phase   from a few seconds to half a minute. It gives place to the clonic phase, in which the tonic spasm of the muscles is succeeded by sharp short interrupted jerks. In this phase the tongue or the inside of the cheek may be caught between the teeth and bitten, and the patient frequently foams at the mouth, the saliva being blood stained if the tongue has been bitten. Incontinence of urine frequently occurs, incontinence of faeces less often.

The clonic phase usually lasts about a minute, the jerking movements becoming less ample and frequent as they die away. During the attack the pupils are usually dilated and fail to react to light. The tendon
Reflexes   reflexes and the plantar reflexes are usually temporarily abolished, and the plantar reflexes are often extensor for a short period immediately after the attack. The corneal reflexes are also lost.

Post-   When the convulsion is over, recovery of consciousness is gradual;
convulsive   the patient is often unconscious for from half an hour to an hour, and
phase   frequently unconsciousness passes into natural sleep. Headache is common after an attack. Usually after recovering consciousness the
'Post-   patient is mentally normal; exceptionally, however, the attack is followed
epileptic   by a phase of 'post-epileptic automatism' during which the patient
automatism'   though apparently aware of his surroundings carries out a series of actions which are often quite inappropriate to the circumstances and of which he afterwards has no recollection. Thus, a housewife after a fit in the middle of the night may get up and lay the table. Crimes of violence are sometimes committed by an epileptic during the phase of post-epileptic automatism. This disturbance of consciousness occurs more often after a minor epileptic attack than after a major attack. Sometimes the patient passes from an attack of epilepsy into an attack of hysteria.

(2)—Minor Epilepsy (*Petit Mal*)

Minor epilepsy is the term applied to attacks characterized by impair-ment or loss of consciousness alone. No hard and fast distinction, however, separates minor from major epileptic attacks. In the slightest minor attacks, or 'sensations', as the patient sometimes calls them, there is a disturbance of consciousness often similar to the aura of a major attack, and the patient may assert that he still remains to some extent aware of his surroundings. In a slightly more severe attack conscious-ness is completely lost. The patient turns pale and pauses in what he is doing; if standing, he continues to stand; his eyes are open, fixed, and staring, and if addressed he makes no reply. After a few seconds he recovers consciousness and continues with what he was doing as though nothing had happened. In somewhat more severe attacks which are transitional in character between minor and major epilepsy the postural and motor functions are affected, and the patient on losing consciousness falls to the ground, or may exhibit slight muscular rigidity, or carry out a stereotyped movement.

(3)—Other Types of Attack

A Jacksonian attack is due to the gradual spread of the disturbance *Jacksonian* underlying the convulsion over the surface of the motor cortex of the *epilepsy* precentral convolution. Hence the convulsion begins with a sharply localized clonic movement of part of the body, for example, the thumb or the lower part of the face, and the movement gradually spreads to involve other parts of the same side of the body in the order in which they are represented in the opposite precentral convolution. In this way, after half a minute or more the whole of one half of the body may become convulsed. The convulsion may then subside, or it may spread to the opposite side of the body, in which case consciousness is usually lost. Partial Jacksonian attacks may occur in which the convulsion is limited to a small part of one side of the body without loss of consciousness. Such a limited convulsion may be continuous and is then known as 'epilepsia partialis continua'. Jacksonian epilepsy is very likely to be followed by transitory weakness of the part of the body first affected *Todd's* in the convulsion, a phenomenon known as Todd's paralysis. *paralysis*

Sensory convulsions consist of paraesthesiae, such as numbness, ting- *Sensory* ling, or 'electric shocks', less often a painful sensation referred to part *convulsions* or the whole of one side of the body. Such a sensation may spread in a manner similar to that of the clonic movements of the Jacksonian attack and in such a case usually indicates that the epileptic disturbance is situated in the opposite post-central convolution. Sometimes the abnormal sensation is followed by clonic movement as the disturbance spreads to the precentral convolution. As in the case of a Jacksonian attack consciousness may be retained or lost.

An uncinate convulsion is a form of sensory convulsion in which the *Uncinate* epileptic disturbance originates in the cortical centre for smell, in the *convulsions* uncinate gyrus, or the closely-related cortical centre for taste. Such an attack is characterized by an hallucination of smell or taste which is usually of an unpleasant nature such as a pungent smell of something burning. The hallucination is often accompanied by convulsive movements of the lips, tongue, and jaw, that is, chewing and tasting movements, which are physiologically linked with the senses of smell and taste. Consciousness is impaired or lost and the patient looks dazed but does not usually fall. A peculiarity of the uncinate attack is that it is frequently associated with a subjective disturbance of memory or the appreciation of time. Thus the patient may experience a feeling that present events have happened before, the '*déjà vu* phenomenon'. More rarely he lives through again in a few seconds long tracts of his past life.

The term 'reflex epilepsy' is used to describe attacks which are con- *Reflex* stantly precipitated by the same external stimulus, which is specific for *epilepsy* each patient. The commonest of such stimuli are cutaneous or auditory. Washing the hands in cold water, standing upon a cold floor with bare feet, touching crumbs with the finger-tips were the exciting stimuli of convulsions in three of my patients. Another who suffered from uncinate

Acoustico-
motor
epilepsy

attacks might precipitate one of them by cleaning her teeth. Epilepsy excited by an auditory stimulus, such as a loud sound, is sometimes known as 'acoustico-motor epilepsy'. In such cases the effectiveness of an external stimulus in precipitating an attack is probably due to the afferent im pulses to which it gives rise impinging upon an area of the cerebral cortex which is already over-excitable. Similarly, a voluntary movement carried out by the patient may precipitate an attack; thus a patient whose attacks began with a rotation of the head to the right found that if he volun tarily carried out this movement an attack might occur.

Reflex
inhibition

Reflex inhibition of a fit is an allied phenomenon. When a convulsion has a focal onset and begins with movement of a limb, a strong stimulus, such as a firm grip, rubbing, or passive movement applied to the limb as soon as the attack begins, may succeed in aborting it.

Inhibitory
epilepsy

Inhibitory epilepsy is the term applied to a rare form of recurrent attack in which there is a transitory loss of power in a limb or in one half of the body, with or without loss of consciousness. Such attacks may alternate with attacks of movement in the affected part.

Tonic fits

Tonic fits, originally called by Hughlings Jackson 'cerebellar fits', have been regarded as being physiologically equivalent to decerebrate rigid ity in man. Consciousness is lost and the patient assumes an attitude of tonic extension of the neck and both upper and lower limbs; the wrists and fingers, however, are flexed. Tonic fits may be produced either by a lesion which interrupts the conductivity of the upper part of the mid- brain, such as a neighbouring tumour, or by any condition, whether neoplastic, inflammatory, or degenerative, which extensively depresses the functions of the cerebral hemispheres.

Myoclonus
epilepsy

Myoclonus epilepsy is a very rare familial disorder first described by Unverricht in 1891. Epileptic fits beginning about the age of ten are followed after several years by symmetrical shock-like myoclonic con- tractions of the muscles of the limbs, which are not attended by loss of consciousness but produce jerking movements of the limb segments and may throw the patient to the ground. The condition terminates in dementia.

5.—THE TIME RELATIONSHIP OF ATTACKS

428.] The frequency of epileptic attacks varies within a very wide range. Some patients have only one or two attacks in a life-time, others are convulsed several times a day. Often minor attacks precede major attacks by several years; but a patient may have either minor or major attacks alone, or the two may alternate. In Gowers' series 76 per cent of patients had attacks at intervals of less than a month. The term pykno-

Pyknolepsy

lepsy has been applied to a variety of epilepsy occurring in children and characterized by the frequent occurrence of minor attacks, up to a hundred or more in a day. The disorder develops suddenly, responds little to treatment and is said to cease spontaneously. It is doubtful

whether there is any good reason for separating pyknolepsy from *petit mal* with less frequent attacks (see PYKNOLEPSY).

Time of day is a factor of importance in determining the onset of *Time of day* epileptic attacks. In 42 per cent of a series of cases attacks occurred by night only, in 24 per cent by day only, and in the remainder both by day and by night. Nocturnal fits are most likely to occur shortly after going to sleep or between 4 and 5 a.m. The commonest time for diurnal fits is during the hour following awakening. Menstruation frequently determines the occurrence of attacks in women, a fit usually occurring just before, less often during or just after the menstrual period.

When the epileptic patient has a series of attacks in quick succession *Serial* but with recovery of consciousness between each, this is known as serial *epilepsy* epilepsy. Sometimes, however, a series of fits occur without intervening *Status* recovery of consciousness—status epilepticus. This is always a serious *epilepticus* condition since unless the fits can be arrested coma deepens, pyrexia or hyperpyrexia develops, and death follows. Very rarely an equivalent condition of progressive coma occurs in epileptics in the absence of an increased number of fits and terminates fatally. Some patients exhibit a special tendency to status epilepticus and develop this condition repeatedly.

6.–MENTAL AND PHYSICAL ABNORMALITIES IN EPILEPTICS

429.] Epilepsy is a disorder of function which may not be associated with any other discoverable abnormality. In fact most patients with idiopathic epilepsy are normal mentally and physically apart from the attacks. Mental disorder may be associated with epilepsy in three ways. (1) The *Mental* mind may be temporarily disordered in association with the attacks. *abnormalities* Post-epileptic automatism is a disorder of this kind. Some epileptics are liable to commit acts of violence during the period preceding an attack. Some after a long series of attacks are mentally confused for days or even weeks. (2) Progressive dementia is the fate of a small proportion of epileptics. Though sometimes attributed to prolonged administration of sedative drugs, it is more probably the result of some endogenous degeneration linked with the cause of the attacks. (3) Mental abnor- *Mental* mality may be a symptom of an organic lesion of the brain to which the *deficiency* epilepsy is also due. In this way mental deficiency may be associated with epilepsy following a birth injury or in cases of tuberous sclerosis.

Physical abnormalities in the nervous system like mental abnormalities *Physical* are usually absent. Slight abnormal physical signs, however, are not *abnormalities* uncommon, such as nystagmus, facial weakness, diminution, especially asymmetrical diminution, of the abdominal reflexes, inequality of the tendon-jerks, and an extensor plantar response on one or both sides. These signs do not indicate progressive disease but lesions acquired in early life, possibly in some cases during intra-uterine life. In fact they

may be mild degrees of the lesions responsible for infantile hemiplegia and congenital diplegia with which epilepsy may be associated.

Endocrine disturbance

Signs of disturbed endocrine balance are not rare in epileptics. Many adolescent epileptics are abnormally tall for their age, and sexual development is sometimes a little precocious in such individuals. On the other hand obesity and genital hypoplasia are sometimes observed. In fact epileptics tend to be, in Kretschmer's phrase, 'dysplastic'. Scars of injuries caused by falls are often seen on the face, and small scattered patches of brown pigmentation are seen in the skin more often than in normal individuals. A facial naevus may be associated with an angioma of the cerebral cortex on the same side, which may cause epilepsy with or without hemiplegia (Sturge-Weber's syndrome).

Sturge-Weber's syndrome

No characteristic abnormality is found in the cardiovascular system, lungs, or abdomen, and no constant metabolic abnormality has been demonstrated. I have twice seen epilepsy and bilateral cataract developing simultaneously in middle life.

The cerebro-spinal fluid

The cerebrospinal fluid is usually normal, but in 20 per cent of cases its pressure is over 200 mm. of fluid, and in the same proportion the protein content of the fluid is above the upper limit of normal.

Radiography of the skull

Radiography of the skull usually does not show any abnormality. Rarely calcification is present in the falx, or in a tumour, especially an angioma, when such is the cause of the attacks. Ventriculography and encephalography, i.e. radiography after the introduction of air into the cerebral ventricles, may demonstrate dilatation of the ventricles or of the subarachnoid space overlying an area of the cerebral cortex. Traumatic epilepsy may be associated with scar tissue uniting the brain to the dura mater, and this may cause a process of the ventricle to be drawn towards the skull and to be demonstrable by encephalography.

7.—PROGNOSIS

Risks of death

430.] The risk of death as a result of an epileptic attack is slight. The attack is self-limited and can prove fatal only through an accident. For instance, a patient who has an attack during sleep may turn over in bed and be asphyxiated by the pillow. Water, fire, machinery, and traffic may prove fatal to an epileptic. Apart from fatal accidents the epileptic patient may sustain minor injuries through falling when unconscious, and recurrent dislocation of the shoulder or more rarely of the jaw may occur in the fits. I have seen one patient, an elderly man, whose first convulsion produced a fracture-dislocation of both shoulders. Status epilepticus may prove fatal if the convulsions cannot be arrested, and even after the cessation of the fits coma may continue and the patient may die with a terminal hyperpyrexia.

Symptomatic epilepsy

The prognosis of symptomatic epilepsy is to a considerable extent that of the underlying cause. The removal of a meningioma, for example, may stop the attacks. Similarly, good results have been claimed for the

surgical excision of a scar in the brain in cases of traumatic epilepsy. In general if nothing can be done to relieve the causal condition the attacks are likely to continue, but even in such cases amelioration and sometimes abolition of the attacks may be brought about by medical treatment, for example in infantile hemiplegia, or cerebral arteriosclerosis. Conversely, serological success in the treatment of neurosyphilis may fail to cure epilepsy of syphilitic origin. Epilepsy associated with mental deficiency is unlikely to be cured.

The prognosis of idiopathic epilepsy depends upon a number of factors. *Idiopathic* In order that the patient may be freed from the attacks it is necessary *epilepsy* to abolish them by treatment for a sufficient length of time for the patient to lose what may be termed the epileptic habit. Perseverance is therefore essential, and thorough treatment should be continued for at least three years after the attacks have ceased. The prognosis is naturally better the sooner treatment is begun after the onset of the attacks. Patients in whom the fits begin after the age of twenty usually do better than those with an earlier age of onset; but these, unfortunately, are the exceptions. A family history of the disease does not necessarily influence prognosis adversely. Patients with frequent severe fits are least likely to be cured, but when the attacks are less frequent major epilepsy often responds better to treatment than *petit mal*. According to Gowers the outlook is best when the attacks occur only during sleep. Marked mental deterioration makes the outlook worse.

The 'cure' of epilepsy must be interpreted as meaning the abolition of the attacks for a period of three years under treatment and subsequent freedom from attacks without treatment up to the present time; for there is always a liability that the attacks may recur at some future date even after a period of freedom lasting for many years. It is difficult to obtain reliable figures as to the proportion of patients in whom a cure interpreted in this sense can be achieved. The prognosis is worse in patients in institutions, since these are largely filled by those who are severely affected and those in whom epilepsy is associated with mental deficiency. Lennox quoted the results obtained in 6,404 patients discharged from the Craig Colony, New York, during thirty-five years. Of these 3 per cent had had no seizures for two years or longer, 15 per cent were discharged improved, 28 per cent were not improved, and 54 per cent died. Non-institutional patients would certainly show a much higher percentage of recovery. Many of these fail to return for treatment when the attacks cease, and are thus lost sight of. In this group of patients freedom from attacks for an indefinite period probably occurs in at least 30 per cent and possibly in a higher proportion. The mortality from epilepsy is highest in young children, in those having frequent major attacks, especially those with a liability to status epilepticus, and in those with marked mental defect. Lennox stated that in a recent year the mortality of patients in Craig Colony was 47 per thousand or about four times that for the general population.

The doctor is often consulted as to the advisability of marriage for *Marriage*

epileptics. As a rule the female epileptic is not adversely affected by marriage. Sometimes the seizures are less frequent during pregnancy and may even be temporarily abolished. Occasionally they are made worse. The risk of transmitting the disorder to children must be individually assessed in each case. This is greatest when the presence of other cases in the family indicate an inherited tendency to the disorder; when, as occasionally happens, there are cases of epilepsy in the families of both partners to the marriage, the risk of the disorder occurring in one or more of the children is considerable. When one parent only is affected, the risk that a child will be affected is not more than about 1 in 10.

8.—DIAGNOSIS

(1)—Differential Diagnosis

431.] The first step in diagnosis is to distinguish epilepsy from other disorders which may simulate it. When it has been established that the patient is suffering from epilepsy the next step is to try to discover its cause. Broadly speaking there are two classes of disorders with which epilepsy is likely to be confused: (i) those characterized by convulsive or spasmodic phenomena, such as hysteria, tetany, tetanus, and strychnine poisoning, and (ii) those characterized by sensory disturbances or altered states of consciousness, such as migraine, aural vertigo, syncope, narcolepsy, cataplexy, vasovagal attacks, and anxiety states.

Diagnosis from hysterical convulsions　　There are fashions in neurosis, and hysterical convulsions are less common to-day than formerly. A hysterical convulsion, unconscious though its origin may be, is nevertheless a dramatic performance demanding an audience. It does not occur therefore when the patient is alone, and may be evoked by a shock or a situation of mental stress. The onset of the attack is more gradual than in epilepsy, and the patient in falling to the ground takes care not to injure herself. Alternate laughing and crying or the utterance of words or phrases takes the place of the epileptic cry, and the movements which comprise the convulsion are of a higher order than the clonic jerks of epilepsy, consisting of voluntary movements such as tearing at the hair or clothes or clutching at bystanders or rolling on the ground. If there is a tonic phase it is commonly a complex attitude, such as opisthotonos or the attitude of crucifixion. Though consciousness is disturbed the hysterical subject, unlike a patient with major epilepsy, is never completely unconscious. The corneal reflexes are preserved, and attempts to open an eye evoke a spasm of the orbicularis oculi. That the patient remains aware of her surroundings is shown by the success of firm handling in terminating the convulsion. Finally the tongue is not bitten in a hysterical fit, nor is the urine passed unless the hysteric has mixed with epileptics, in which event this symptom may be reproduced.

From tetany and other spasmodic disorders　　Tetany is readily distinguished by the characteristic intermittent attacks of carpo-pedal spasm (see CONVULSIONS IN INFANCY AND CHILDHOOD, Vol. III, p. 420) in which consciousness is not lost. In tetanus there is

persistent muscular spasm which usually causes trismus early, spreading
later to other parts of the body and intensified by periodical exacerba-
tion. In this disorder also consciousness is retained. In strychnine poison-
ing a history of poisoning can usually be obtained. The convulsions *From*
are reflexly excited and in spite of their violence the patient remains *strychnine poisoning*
conscious, whereas epileptic convulsions of equal severity are always
attended by loss of consciousness. In rabies there is almost always a *From*
history of a bite from a rabid animal. In this disorder the general con- *rabies*
vulsions are preceded by the characteristic pharyngeal spasm which is
brought on by the attempt to drink and is quite pathognomonic.

In migraine the development of symptoms is always much more gradual *From*
than in epilepsy. Both the visual symptoms and the paraesthesiae take *migraine*
from ten minutes to half an hour to develop in contrast with the aura of
epilepsy which develops in a few seconds. The cortical symptoms of
migraine, moreover, are almost always followed by headache, and the
patient remains conscious throughout the attack. Occasionally, however,
as stated above, an attack of migraine in certain individuals terminates
in an epileptic convulsion.

Aural vertigo may be confused with *petit mal* in which also giddiness *From aural*
may occur. But in vertigo of aural origin other symptoms of aural *vertigo*
disease, namely, tinnitus and deafness, are usually present and the
giddiness usually lasts much longer than in *petit mal*. Though aural
vertigo may cause the patient to fall, consciousness is retained save very
rarely in cases of extreme severity (see VERTIGO).

Syncope, which may also be confused with *petit mal*, usually occurs *From syncope*
either in weakly adolescents with vasomotor instability or in persons
subjected to severe shock or suffering from profound anaemia as a
result of haemorrhage. Both the onset and the cessation of a syncopal
attack are more gradual than is usual in *petit mal*, and in syncope the
patient is limp, whereas *petit mal* is more likely to be accompanied by
slight muscular rigidity. The so-called vasovagal attacks, which usually *From*
occur in women, are characterized by symptoms of disturbance of *vasovagal attacks*
function of the autonomic nervous system. These attacks develop more
gradually than epileptic attacks, usually beginning with abnormal feelings
referred to the head or the abdomen. These are followed by coldness
of the extremities and lowering or increase of the pulse-rate, and the
patient experiences a feeling of weakness, distress, or even, in severe
cases, of impending death. There is as a rule no loss of consciousness in
a vasovagal attack, which may last from a few minutes up to half an
hour (see BRAIN: VASCULAR DISORDERS, Vol. II, p. 642).

Sufferers from anxiety neurosis are sometimes subject to 'anxiety *From anxiety*
attacks' which are characterized by trembling, sweating, palpitation, *attacks*
and a vague sense of fear. There is, however, no loss of consciousness,
and convulsions are absent.

Narcolepsy and cataplexy, which may both occur in the same indi- *From*
vidual, may be confused with epilepsy, since in narcolepsy consciousness *narcolepsy and*
is lost and in cataplexy the patient may fall to the ground. Narcolepsy *cataplexy*

is physiologically identical with sleep, from which it differs only in its irresistible onset however inappropriate the circumstances. Convulsions are absent, and the patient though unconscious can be immediately aroused by appropriate stimuli as from normal sleep. Cataplectic attacks are usually excited by strong emotion and, though the patient is temporarily deprived of muscular tone and power, the condition is distinguished from epilepsy by the retention of consciousness (see NARCOLEPSY).

(2)—Diagnosis of Causes

When the diagnosis of epilepsy has been established, the next step is to ascertain if possible the cause of the attacks. In this connexion the age of the patient is so important that it is convenient to consider the diagnosis of the causes of epilepsy in relation to the patient's age.

Convulsions in childhood In childhood, infantile hemiplegia and congenital diplegia give rise to no difficulty. The convulsions associated with teething, rickets, and acute infections are also usually readily recognized. When convulsions are a symptom of acute encephalitis, a series of fits occurs in a previously healthy child and is associated with fever and often with coma and the development of hemiplegia. In the rare cerebral degenerative disorders of childhood there is progressive mental failure associated with the gradual onset of diplegia and sometimes blindness. In tuberous sclerosis epilepsy is linked with mental defect and the eruption of adenoma sebaceum over the face.

In adolescence and adult life Between the ages of seven and twenty idiopathic epilepsy is far the commonest cause of convulsions. If epilepsy begins after the age of thirty, the attacks should be presumed to be of organic origin until all such causes have been excluded.

Intracranial tumour In adult life intracranial tumour is a common cause of convulsions which may precede other symptoms and signs by several years. The diagnosis is easy if signs of increased intracranial pressure are associated with signs of a progressive focal lesion of the brain. In the absence of these, radiography of the skull and ventriculography or encephalography may be necessary to demonstrate the presence of a tumour. In most cases in which a cerebral tumour causes epilepsy the patient is between thirty and fifty-five years of age.

Neuro-syphilis Neurosyphilis, especially dementia paralytica, accounts for a proportion of cases in which epilepsy first appears in adult life. The coexistence of the physical signs of neurosyphilis, especially of Argyll Robertson pupils and of a positive Wassermann reaction in the blood and cerebrospinal fluid, in most cases settles the diagnosis.

Cysticercosis Cerebral cysticercosis as a cause of epilepsy is recognized by the presence of cysticerci elsewhere in the body, especially subcutaneous and intramuscular (see CYSTICERCOSIS, Vol. III, p. 523).

Traumatic epilepsy When head injury is suspected as a cause of epilepsy, special attention should be paid to the occurrence of focal symptoms at the onset of the attacks, and encephalography should be carried out to ascertain if there

is evidence for the presence of a scar in the brain causing traction on part of the ventricular system.

Convulsions as a symptom of hypertensive encephalopathy may occur *Hypertensive* in acute nephritis, malignant hypertension, and eclampsia. In all these *encephalo-* conditions the blood-pressure is likely to be raised and retinal oedema *pathy* and exudation are usually present. Albuminuria occurs in acute nephritis and eclampsia but not always in malignant hypertension.

Epilepsy caused by cerebral arteriosclerosis occurs in late middle *Cerebral* life and old age and may or may not be associated with a raised blood- *arterio-* pressure. Thickening and tortuosity of the retinal arteries and arteries of *sclerosis* the limbs are usually present, and the patient is likely to manifest other symptoms of cerebral arteriosclerosis, such as impairment of memory and emotional instability, and in some cases signs of focal cerebral vascular lesions.

9.–TREATMENT

432.] As far as possible the patient should lead a normal life. Seizures *General* are more likely to occur during idleness than during occupation. A *management* regular occupation is therefore very desirable. Epileptic children should *Occupation* if possible attend an ordinary school where their disability will receive sympathetic understanding and should be subjected to ordinary dis- cipline. The adult epileptic should carry on an occupation or trade in which he is not exposed to risk on account of his liability to attack. Occupations involving work at heights or in close contact with machin- ery will necessarily be ruled out. As a driver of a motor car the epileptic is a danger both to others and to himself, and in Great Britain every person applying for a driving licence is required by law to state whether or not he is subject to attacks of unconsciousness or to epilepsy. It is impossible to protect an epileptic entirely from the risks of everyday life to which his disorder exposes him, but these should be explained to the patient and his friends, and he should be advised not to bathe alone. Moderate exercise is advantageous, but violent and exhausting exercise sometimes precipitates an attack. The general health should be main- tained at as high a level as possible. The diet should be varied and *Diet* constipating food avoided. Many epileptics are apt to eat voraciously, and this tendency should be curbed. When the attacks are liable to occur in the early morning, a light meal such as sweetened milk and biscuits should be taken at bedtime and a similar meal immediately on awakening. Constipation may precipitate attacks and care should be taken therefore that the bowels are opened daily.

It is often impossible to care adequately at home for patients having *Institutional* frequent severe attacks and for those in whom epilepsy is associated *care* with gross mental defect. Such patients must be admitted to suitable institutions, and many have far fewer attacks in an epileptic colony than in any other surroundings.

The object of treatment with anticonvulsant drugs is if possible to

*Treatment
with drugs*

suppress the attacks long enough for the patient to lose the epileptic habit. To achieve this end it is necessary to give the drugs in doses sufficient to suppress the attacks and to continue thereafter until the patient has been free from seizures for three years. When the attacks occur fairly regularly at certain times of the day or of the month, it is generally desirable to arrange the doses so that the maximum dose is given a little before the time at which the attacks are most likely to occur. Thus, when the attacks are nocturnal or occur in the early morning, a single dose taken at bedtime is sometimes sufficient to suppress them. Similarly, when the attacks occur only at the monthly periods, it is sometimes sufficient to confine the administration of drugs to a week before and a few days immediately following the period. Not uncommonly, however, such measures merely postpone the attack, and it is then necessary, as is always the case when the attacks occur at irregular intervals, to give the drugs regularly two or three times a day.

Bromides

For many years bromides were the only effective drugs in the treatment of epilepsy, and they are still of considerable value. Combinations of bromine with various bases have been tried, but there is little evidence that one is more effective than another or that a combination of brom-ides is more useful than a single salt. Sodium bromide is probably less depressing than potassium bromide, but calcium bromide does not seem to present any special advantages. It is usually wise to begin treat-ment with bromide before trying other remedies. Potassium or sodium bromide 10 grains three times a day, or 15 grains night and morning, are suitable commencing doses for an adult, and in any case the total daily dose should not exceed 60 grains. The action of bromide is rendered more effective if the patient's intake of chlorides in the form of common salt is restricted. The bromides are constipating, depressing, and apt to lead to acne. It is therefore usually necessary to give aperients to patients who are taking bromide, and the depression can to some extent be combated by the administration of tincture of nux vomica in 10 minim doses with each dose of bromide. The tendency to acne can be diminished by giving 3 minims of arsenical solution with each dose, but this should be omitted for one week in every four.

Barbiturates

The barbiturates have proved a very effective weapon in the treatment of epilepsy and may be given either alone or in combination with bromide. Phenobarbitone (luminal or gardenal) is a derivative of barbi-tone (veronal). It is practically insoluble in water and is usually given in tablet form, but the sodium salt, phenobarbitone-sodium, is readily soluble, though it is incompatible with ammonium salts and with acids. Phenobarbitone is more effective in the treatment of major epilepsy than of *petit mal*. When bromide alone in full doses does not control the seizures, it is convenient to give phenobarbitone in addition, begin-ning with a dose of $\frac{1}{2}$ grain night and morning and, if necessary, increas-ing up to a total dose of 3 grains a day. Patients with an idiosyncrasy to this drug may develop an extremely irritating erythematous or urticarial rash, and in toxic doses the drug may lead to headache, vertigo,

lethargy, and impotence, and even to ataxy and mental confusion. Phenobarbitone should never be withdrawn suddenly, owing to the risk of an increase in the number of seizures. Its withdrawal should always be covered by increasing doses of bromide or some equivalent drug. Prominal (N-methylethylphenylmalonylurea) is usually much less effective than phenobarbitone. It is given in larger doses, namely 3 grains, two or three times a day, and as much as 15 grains a day is sometimes well tolerated. Superminal, the calcium salt of dibromethylbarbituric acid, is sometimes more effective than either bromide or phenobarbitone. It is given in doses of 0·5 gram, either alone or in combination with phenobarbitone or bromide.

Other drugs are of value only as adjuvants to those already mentioned. Tincture of belladonna in doses of from 5 to 10 minims is sometimes useful for the treatment of *petit mal*, and borax may be given in combination with bromide in doses of 10 to 30 grains three times a day. Endocrine preparations are of little value, but the ovarian follicular and *Hormones* luteal hormones may be given a trial in women in whom the seizures occur only at the menstrual periods, especially when there is menstrual irregularity.

When a patient develops status epilepticus, the lower bowel should be *Treatment* well washed out with enemas, and rectal salines must be given if uncon- *of status* sciousness is prolonged. As early as possible 5 grains of phenobarbitone- *epilepticus* sodium in 25 per cent solution should be given either subcutaneously or intravenously, and this is usually effective in cutting short the attacks. The same dose can be repeated if necessary. An alternative method of treatment is to administer 60 grains of chloral hydrate or sulphonal in solution or 1 fluid ounce of paraldehyde by the rectum. If the convulsions continue in spite of sedative drugs light chloroform anaesthesia should be used to control them.

The observation that complete starvation caused a marked reduction in the number of fits in epileptics led to the treatment of epilepsy by means of a ketogenic diet on the assumption that the effective factor in the starvation was the resulting ketosis. A ketogenic diet is a diet rich *Ketogenic* in fats and poor in carbohydrates, and its administration leads to the *diet* presence of ketone bodies in the urine. This diet has been found to be of some value in the treatment of epilepsy in children, abolishing the attacks in about 30 per cent of cases, while in a further 20 per cent the frequency of the attacks is reduced. The diet is calculated in terms of the ratio of ketogenic (fat) to antiketogenic (protein and carbohydrate) substances in the foodstuffs. This is described as the ketogenic : antiketogenic ratio. It is usual to begin with a ratio of 2:1, increasing it as necessary up to 4:1, the urine being examined daily for acetone and acetoacetic acid. The patient is kept on the diet of minimum ratio necessary to control the attacks. Vitamin deficiency must be guarded against by giving marmite, cod-liver oil, and fresh tomato daily. Since the ketogenic diet is unpleasant and is effective only so long as it is strictly adhered to, it has never been very widely adopted. The same

applies to the method of treatment by drastic restriction of the patient's intake of water.

Surgical treatment   The surgical treatment of epilepsy by trephining the skull probably originated in prehistoric times. At present its scope is restricted to those cases in which there is clear evidence of an organic lesion of the brain which can be successfully removed, such as intracranial tumour, and some cases of traumatic epilepsy, for the treatment of which it is still on trial. Foerster and Penfield recommend surgery in cases in which epilepsy follows a head injury, provided that there is clear evidence of a focal origin for the attack and that ventriculography demonstrates displacement of the ventricular system towards the lesion or meningeal adhesions superficially to it. In such cases wide excision of scar tissue from the affected area of the brain may be effective in abolishing the attacks, but such a procedure should only be considered when medical measures have been given a reasonable trial and when the requisite indications are present. Indiscriminate operations on the skull and excision of the cervical sympathetic chain are useless.

Treatment of symptomatic epilepsy   The treatment of symptomatic epilepsy is primarily that of the under lying cause. In addition, treatment with anticonvulsant drugs should be carried out on the same lines as for idiopathic epilepsy.

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EPILOIA

SECTIONS 1, 2, AND 4 TO 7

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1.—DEFINITION

(*Synonyms.* Tuberous sclerosis; Bourneville's disease, Brushfield and
Wyatt's disease)

433.] Epiloia is a disorder characterized by the presence of small firm
nodules in the brain, a condition to which the term tuberous sclerosis
has been applied, and of tumour-like masses in the eye (phakoma-), the
heart (rhabdomyomas), kidneys, and sometimes other viscera, and by
an eruption on the nose and cheeks, adenoma sebaceum. These
abnormalities are congenital and sometimes familial. They are not all
present in every case; but in the fully-developed form, to which the
term 'epiloia' has been applied, the patient suffers from epilepsy which
usually begins in infancy, is mentally defective, and exhibits the
characteristic eruption, adenoma sebaceum, over the nose and face

Historical   Bourneville and Brissaud in 1880 first described the cerebral lesion
of tuberous sclerosis. Bourneville's patient exhibited the fully developed
syndrome of mental defect, epilepsy, and adenoma sebaceum, though
the last-named was regarded as a coincidence. Adenoma sebaceum was
described by Balzer in 1885 and by Pringle in 1890. The relation between
the cutaneous and other lesions was gradually established and the term
epiloia was applied to the whole syndrome by Brushfield and Wyatt in
1926. The retinal lesions were described by van der Hoeve in 1923.

2.—AETIOLOGY

There has been some discussion whether the lesions of epiloia should
be regarded as congenital dysplasias or as true neoplasms. Their wide
distribution in different tissues of the body, their non-progressive
character, their association with other congenital abnormalities, and
their familial incidence in some cases are all in favour of the view that
they are congenital dysplasias. That they occasionally undergo a meta-
plasia into a true neoplasm is not inconsistent with this conclusion, since
this change is well known to occur in other congenital abnormalities.
Heredity   Multiple cases of epiloia in one family either in its complete or in its
abortive form are not uncommon and would seem to imply that it is
the outcome of a germinal abnormality which is sometimes inherited.
Penrose suggests that it is probably due to a single dominant gene
which is subject to modification by autosomal genetic factors. There is
nothing in support of the view that congenital syphilis, birth trauma,
or other exogenous factors are of aetiological importance, and it
would seem that if present these could be no more than precipitating
factors.

3.–MORBID ANATOMY

(1)—Tuberous Sclerosis of the Brain
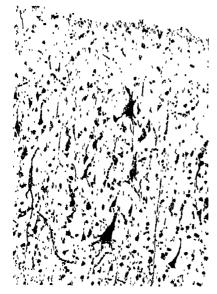
The lesions in the brain differ greatly in extent, but are remarkably *Macroscopic* constant in their characters. They consist of localized areas of sclerosis *appearances* of the cortex, and of firm rounded protrusions on the walls of the lateral and third ventricles resembling 'candle gutterings'. The brain in the fresh *Localization* state at first sight appears normal externally, but on careful examination *of lesions* certain convolutions are paler and wider than normal and feel abnormally hard. On section the distinction between grey and white matter is not very evident in the affected convolutions, and the sclerosis can be felt to affect the white as well as the grey matter. The sclerosis may involve single convolutions or an area composed of several neighbouring convolutions or, on the other hand, only a limited area in a convolution. In some cases these areas are extremely numerous so that half the cortex of the brain is affected, whereas in slight cases only one or two restricted areas of cortical sclerosis can be seen, most commonly in the frontal and temporal lobes. After fixation by formalin the sclerotic areas are even paler and firmer than in the fresh state and, as they shrink less than the normal cortex, they tend to stand out on the surface as pale tuber-like masses, an appearance from which the name 'tuberous sclerosis' is derived. But in the fresh state they are not raised above the other convolutions, unless there has been long-standing malnutrition with general atrophy of the brain; nor do they disturb the normal convolutional pattern.

The 'candle gutterings' in the ventricles most often run down between *'Candle* the head of the caudate nucleus and the thalamus. In this situation they *gutterings' in* may be raised a quarter of an inch above the normal level of the *ventricles* ventricular wall. They are white, firm, smooth, and rather lobulated. Smaller similar projections may be seen in the posterior horns of the lateral ventricle and occasionally in the iter of Sylvius and fourth ventricle. Less often small rounded sclerotic areas can be felt in the substance of the basal ganglia, especially the thalamus, or in the white matter of the centrum semi-ovale. Very rarely they are found in the cerebellum. These are sometimes described as small tumours, but probably the majority are in a static condition and are not true neoplasms. True tumours, however, may be present, usually growing from *Tumours* the basal ganglia and projecting into the lateral or third ventricles.

Microscopically the most obvious changes in the sclerotic areas of the *Microscopic* cortex are paucity and disordered arrangement of nerve-cells with *appearances* dense neuroglial sclerosis. The external (molecular) layer is wider than normal. The nerve-cells throughout the cortex are small and widely spaced, the majority resembling more or less undeveloped neuroblasts, but here and there, often in the outer layers, are seen collections of large nerve-cells the size of a Betz cell (see Fig. 10). These are usually arranged radially to the surface, but many are of abnormal shape and

some lie tangentially. There is little evidence of arrangement of the small nerve-cells in definite layers and the boundary between cortex and white matter is indefinite, since many nerve cells can be seen in the white centre of the convolution. The neuroglial sclerosis consists of a dense meshwork of fibres with occasional greatly enlarged neuroglial cells. This extends throughout the cortex and affects also the white matter of the convolution, fading away as the centrum semi ovale is approached. In this and in the unaffected convolutions there may not be any definite abnormality, or there may be a slight general overgrowth of neuroglial fibres in the white matter and occasional abnormal neurons or neuroglial cells in the apparently normal cortex.

'Candle gutterings'

The 'candle gutterings' in the walls of the ventricles are composed of a dense mass of neuroglial fibres, often with a collection of large rounded or fusiform neuroglial cells in their centre. They may be covered by a layer of ependymal cells, but usually they break through this layer over some part of their extent. They sometimes contain many thick-walled vessels, and calcareous concretions are not uncommon in their centre. The rounded sclerotic areas in the basal ganglia are of similar structure, but here large-bodied neuroglial cells are more in evidence. These may be collected

Basal ganglia

FIG. 10.--A group of giant nerve-cells in the superficial layers of the cerebral cortex in an area of tuberous sclerosis

in small nests or packed close together over a fairly wide area. When they are fusiform their processes form interlacing bundles and whorls, and usually a rather dense feltwork of neuroglial fibres can be seen between the large cells.

True tumours

The true tumours vary greatly in size and in rate of growth as well as in structure. The most common forms are glioblastoma multiforme and polar spongioblastoma, but large-celled astrocytomas and astroblastomas have also been described. In a personal case a very large rapidly-growing tumour apparently of ependymal origin filled the anterior part of one lateral ventricle. Usually, however, the tumours are small, commonly the size of a walnut or a plum, but, owing to their situation, they often lead to hydrocephalus.

(2)—Retinal Nodules

Naked-eye appearance

The retinal phakomas are visible to the naked eye as white or greyish, irregularly rounded areas. Two, three, or more are often present in each

eye. They usually lie in the posterior pole of the retina and commonly overlie the disc, but their situation is capricious.

Under the microscope a phakoma appears as a lenticular nodule *Microscopic appearance* of cellular or loosely areolar neuroglial tissue, lying in the innermost layer of the retina and bulging the internal limiting membrane inwards (see Fig. 11). The outer margin of the nodule reaches the inner granular layer which may be compressed or destroyed but is often remarkably healthy. In addition to the tangle of fusiform neuroglial cells with strong fibres, which form at least the marginal parts of the nodule, there may be

FIG. 11.—A nodule of neuroglial tissue in innermost layer of retina, in a case of epiloia

found in its centre collections of large rounded cells with clear cytoplasm and eccentric nucleus, similar to those already described as occurring in the nodules in the basal ganglia. Calcified spherules are sometimes seen in the centre of the nodule. The resemblance of the nodules in the retina to those in the basal ganglia and in the walls of the ventricles is thus very close.

(3)—Rhabdomyomas of the Heart

These are small discrete whitish *Size* nodules, lying in the muscle and varying in size from that of a millet seed to that of a pea or a bean. The larger masses are usually seen in infants, and may then form the greater part of the bulk of the heart. They have been found at all *Histology* ages, but their histological appearance changes with growth, the characteristic cells seen in infantile cases probably being replaced by fibrous and fatty tissue as age advances. In the infant the nodule consists of large cells with foamy or striated cytoplasm, containing

FIG. 12.—The edge of a rhabdomyoma of the heart. The rhabdomyoma is seen to consist of large clear cells with a central nucleus which is surrounded by a faintly-stained zone of cytoplasm. Fine connective-tissue fibres separate the individual cells. Above is a layer of normal muscle-fibres

glycogen but no fat. Each cell is surrounded by a fine capsule of connective tissue (see Fig. 12) and the nodule as a whole may be divided from the normal heart-muscle by a fibrous wall of considerable thickness. In older children and adults fibrous or fatty tissue

forms the greater part of the nodule, only a few of the abnormal large cells remaining towards the centre.

The abnormal cells characteristic of a rhabdomyoma are considered to be a foetal type of heart-muscle cell with a greater or less degree of glycogenous infiltration. Rhabdomyomas of the heart are therefore not true tumours, seeing that they appear to repress rather than to increase in size with the growth of the body. They are found only in cases of tuberous sclerosis of the brain and appear to be as characteristic of epiloia as the lesions in the skin and kidneys, although, probably owing to their small size, they have not been found in such a large proportion of cases.

(4)—Renal Tumours

Tumours of the kidneys are found after death in the great majority of cases of epiloia, although they rarely cause symptoms during life. Very rarely a large tumour of the Grawitz type produces renal symptoms, and cases are described in which tuberous sclerosis of the brain was found, unexpectedly, in patients dying of renal tumours. But most often the tumours are small whitish cortical growths, occurring in large numbers in both kidneys. They vary in histological appearance but appear to be most often fibromas, or fibro-adenomas, arising from undifferentiated elements of the Wolffian ridge. Although the term sarcoma has often been used in describing them they rarely show any evidence of malignancy.

(5)—Adenoma Sebaceum

The skin in the areas affected by adenoma sebaceum presents a microscopical structure which differs only quantitatively from that of normal skin. The epidermis is thinned, the dermal tissues are often more vascular than normal, and the sebaceous glands hypertrophied. True adenomas of these glands, however, do not seem to occur, and the name adenoma sebaceum is to this extent misleading.

(6)—Nature of Epiloia

It is now evident that most of the lesions of epiloia are congenital dysplasias which do not progress during growth. This appears to be true of the tuberous sclerosis of the brain, the rhabdomyomas of the heart, and the majority of the renal tumours. The skin lesions sometimes become visible first during adolescence, but it is likely that they also are congenital abnormalities of the sebaceous glands which only become obvious when the normal adolescent development of these glands takes place. As regards the retinal lesions less is known, as they have seldom been observed over a period of years. If they grow in size it is evident from their structure that this growth is extremely slow. But along with these congenital dysplasias there is a tendency for true tumours to form in both the brain and the kidney. Although these are usually of slow growth, they may be rapidly growing and even malignant.

In a few families the lesions of neurofibromatosis have been associated *Association* with epiloia. Instances of this kind have been very rare and may be *with neuro-* accounted for by the coincidence of two hereditary diseases, and in the *fibromatosis* present state of our knowledge more confusion than clarity seems likely to arise from the attempts made by some authors to bring the two conditions into a close relationship.

4.–CLINICAL PICTURE

It is convenient to describe first the clinical picture of the disease in its fully-developed form, and then to discuss its manifestations in those cases in which its incidence is limited to a smaller number of tissues. In the fully-developed form symptoms are present either from birth or from an early age. Epilepsy is usually the earliest symptom described, perhaps because it attracts attention as soon as it occurs, whereas mental defect is usually not noticed until the child is some months or even a year or two old.

(1)—Epilepsy

Convulsions usually begin during the first year of life. This was the case in thirteen out of the seventeen patients reported by Ferraro and Doolittle. In Hartdegen's case, one of the first to be described, convulsions were noted a few hours after birth and continued until the death of the child two days later. In rare instances the attacks do not begin until late childhood or adolescence or even occasionally adult life. All varieties of epileptic attack have been described, *grand mal, petit mal,* Jacksonian epilepsy, and various epileptic equivalents. The frequency and periodicity of the attacks are very variable. Some patients have many attacks in a day, whereas others have only one or two in a year. Long periods of remission may occur irrespective of treatment. Status epilepticus may be a terminal feature.

(2)—Mental Defect

Mental defect is usually present from the beginning of life, and in such cases attention is drawn to it by the backwardness of the child in sitting, walking, and talking, and its slowness in reaching the usual milestones of development. In some reported cases, however, the early development of the child was apparently normal, but after a few years a progressive deterioration set in. Whether or not the child is mentally defective from the beginning, the mental functions undergo a progressive enfeeblement later. Critchley and Earl pointed out that the essential psychological *Associated* feature of epiloia was a combination of intellectual defect proper with *psychosis* a primitive form of psychosis. The intellectual defect is always pronounced, the patient falling into the group of imbeciles or idiots, and the psychosis is best described as a primitive type of catatonic schizophrenia.

High-grade patients

For descriptive purposes patients may be divided into high and low grades. High-grade patients are usually capable of profiting by some training and may even learn to read and write a little. At or before puberty psychotic symptoms appear, consisting of apathy and seclusiveness varied by outbursts of motiveless excitement. Catatonia, flexibilitas cerea, and even stupor may occur. Speech deteriorates and the patient

Low-grade patients

may become mute. In the low-grade group mental development occurs later and is less complete, and deterioration begins earlier. The psychosis is of a more primitive character and the patient exhibits bizarre attitudes and stereotyped movements. Speech is poorly developed or completely absent. Catatonic rigidity is constant in the later stages, and there may be an apparently complete lack of consciousness of the surroundings.

(3)—The Skin

Adenoma sebaceum

The characteristic cutaneous lesion, adenoma sebaceum, is usually first noticed in early childhood and increases at puberty. Exceptionally it is present at birth or may not appear until early adult life. The

Distribution of rash

rash is distributed over the nose and the middle of the cheeks in the shape of a butterfly (see Fig. 13). The upper lip escapes, but the chin, brow, and temples are sometimes affected. It consists of a papular eruption, the individual nodules being firm and reddish. Each measures about four millimetres in diameter. Over the nose they are often confluent. Telangiectases are present in the centres

Other skin lesions

of the nodules.

FIG. 13.—Photograph of patient with epiloia, showing adenoma sebaceum. (Kindly lent by Dr. R. M. Stewart)

Other cutaneous lesions are not uncommon and include patches of brown pigmentation similar to those met with in von Recklinghausen's disease, small flat cutaneous fibromas, pedunculated cutaneous fibromas or mollusca fibrosa, and naevi.

(4)—Neurological Manifestations

Neurological abnormalities may be altogether absent. Occasionally gross disturbances such as hemiplegia or diplegia are found. Muscular hypotonia is usually present in the earlier stages giving place later to rigidity. In low-grade patients the so-called stigmata of degeneration found in other types of mental defect may be present. Associated congenital abnormalities are sometimes found, including hydrocephalus, which is probably due to obstruction of part of the ventricular system

by intraventricular tuberous sclerosis. In those rare cases in which a true intracranial neoplasm is present the usual signs of this, including papilloedema, are found. Very rarely neurofibromatosis has been found associated with the lesions of tuberous sclerosis in the same patient.

(5)—The Eye

The retinal tumours, first described by van der Hoeve and named by him 'phakomas', are sometimes present but are by no means constant. These are seen in the fundus as flat, white, round or oval areas about half the size of the optic disc, and usually at the posterior pole of the retina, but may overlie the disc. They may be single or multiple.

(6)—Clinical Variants

In addition to the fully-developed form of the disorder incomplete forms occur, the relations of which to the fully-developed form can sometimes be established by the occurrence of both complete and abortive forms in members of the same family. Thus adenoma sebaceum may occur in an individual who is otherwise apparently quite normal, or may be associated with epilepsy but not with mental defect. Another variant is the presence of a visceral tumour, for example a tumour of the kidney or a phakoma of the retina, in the absence of other clinical manifestations of epiloia.

Incomplete syndromes

Visceral or eye tumour alone

5.–COURSE AND PROGNOSIS

The course of the disorder has already been described (see p. 123). Most patients finally reach a mental state comparable with that of an advanced stage of schizophrenia. A few remain stationary at the mental level of a low-grade mentally defective patient. Death occurs early, usually before the age of twenty, although some patients survive into the third and fourth decades. Death is usually due to intercurrent disease or status epilepticus, more rarely to intracranial tumour, visceral tumour, or sudden heart failure.

6.–DIAGNOSIS

In the fully-developed form of the disorder the association of epilepsy, mental defect, and adenoma sebaceum is so distinctive that difficulty in diagnosis is hardly likely to arise, although care must be taken not to mistake the adenoma sebaceum for a bromide rash. In those rare cases in which adenoma sebaceum does not develop until adolescence or later it may be impossible to distinguish the condition from other causes of epilepsy associated with mental defect. The presence of other cutaneous abnormalities, however, especially pigmentation, or of a retinal phakoma, or of other cases of epiloia in the family may provide a clue to the correct diagnosis.

7.—TREATMENT

No treatment influences the mental defect or the progressive mental deterioration. The treatment of the convulsions is that of epilepsy in general (see p. 113). The development of an intracranial tumour may necessitate surgical interference. In most cases the mental defect renders it necessary for the patient to be admitted to an institution.

Institutional treatment

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EPIPHYSES, DISEASES AND INJURIES

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1.—DEVELOPMENT OF EPIPHYSIS

434.] The epiphysis of a bone strictly speaking is that portion which develops from a centre of ossification independent of the main centre of ossification for the shaft of the bone. But it also includes the growth disc of cartilage from which increase in length of the bone takes place. At a later period this growth disc becomes completely converted into bone and the epiphysis thus becomes fused to the main bone. Under certain influences this fusion may be either hastened or retarded, and the change of cartilage into bone may also be affected. Some constitutional diseases, such as rickets, produce these effects and if allowed to continue may permanently affect the growth of the bone.

Any inflammatory condition close to the epiphysial cartilage has an effect upon its development. It may by its intensity permanently damage the cartilage; on the other hand it may when chronic increase the local blood-supply and thereby lead to more rapid proliferation of the epiphysial cartilage and so to an increase in the rate of growth of the bone.

2.—EPIPHYSITIS

435.] Epiphysitis is an inflammation of the epiphysis, the result of an infection by either pyogenic or specific organisms.

(1)—Acute Pyogenic Epiphysitis

Acute infection of an epiphysis is seldom the primary focus of a bone infection. More usually an acute osteomyelitis of the bone starts in the metaphysis close to the epiphysial cartilage and the epiphysitis results from a direct spread of the infection through the damaged cartilage of the growth disc. The most common situation in which this occurs is at the upper end of the femur in an infant.

Infective epiphysitis of femur

The infant is a few weeks or months old when it suddenly becomes seriously ill with signs of arthritis of the hip-joint. The hip is flexed and adducted, so that any attempt to move the hip causes the infant to cry out. The pulse is rapid, and a high temperature and all the other signs of a severe toxaemia are present. Within a few days an abscess develops, and this, though it may track forwards, usually points posteriorly in the buttock. An X-ray of the hip-joint in the early stages is not of any value, but later the neck of the femur may appear to have lost some of its normal density, and a partial subluxation of the hip may be visible. The infant may develop some other focus of disease but usually it does not do so. The diagnosis may be difficult at first though the general disturbance will suggest an acute pyogenic infection. Occasionally, especially in very young children, a tuberculous arthritis may give rise to similar very acute signs and symptoms. An acute inflammatory

adenitis may be mistaken for an arthritis, but in adenitis the general signs are not so severe as in arthritis.

The prognosis is good as regards life, but the child is always left with *Prognosis* permanent damage to the hip-joint. During the acute stage the epiphysis may appear from an X-ray to have entirely disappeared but, when the infection has settled down, a portion is often seen to have escaped destruction. However well these children are treated, the hip always undergoes some amount of subluxation, and the remains of the epiphysis generally articulates with the upper rim of the acetabulum, which is to some extent damaged by the arthritis. The child walks with a very decided limp, and has a very unstable hip-joint and the characteristic scar on the buttock. Reconstructive surgery should not be attempted on such patients. In spite of the very decided limp they can do most things.

Fixation of the limb in abduction with fixed traction is desirable, *Treatment* but it is very difficult to achieve this in an infant, and whatever means are used to maintain the necessary fixation will need to be continually adjusted.

When the abscess is localized it must be incised and allowed to drain. A rubber drain should not be inserted, as this may further damage the bone and will certainly stiffen the joint. The sinus generally heals up quite soon.

(2)—Chronic Pyogenic Epiphysitis

Chronic epiphysitis is not common, but a Brodie's abscess will, as a result of its proximity to the epiphysial cartilage, cause this to proliferate more rapidly, thus producing an increase in length in the affected bone.

(3)—Tuberculous Epiphysitis

This may develop in any epiphysis. The infection may be very acute or so chronic that it is not identified until the neighbouring joint becomes infected. In the acute form destruction of bone takes place quite rapidly and spreads into the joint.

Acute tuberculous epiphysitis may be very difficult to diagnose clinic- *Diagnosis* ally from a pyogenic infection, as the limb will be very painful and tender and the joint rigid with muscular spasm; but such an acute condition is rare at the present day. Sometimes it can be diagnosed only by identification of the organism. In chronic tuberculous epiphysitis rarefaction of the epiphysis due to caries occurs, and this may be such a slow process that considerable damage is done before any signs or symptoms reveal the presence of active disease. It is only when the joint becomes infected that the more chronic underlying bone disease is identified.

A really acute tuberculous epiphysitis will infect the neighbouring *Treatment* joint cavity, and it requires drainage in the same way as a pyogenic *of acute* infection. The limb, as in any other infection, requires fixation and *disease* traction in the position appropriate to the joint infected.

Of chronic disease

When a chronic tuberculous epiphysitis is recognized fixation and traction are required over a prolonged period, until on both clinical and X-ray examination the disease is shown to be quiescent; thereafter the affected limb or joint must be guarded against strain for a further period.

(4)—Syphilitic Epiphysitis

The provision by the State of free and adequate treatment for syphilis has resulted in syphilitic epiphysitis becoming rare. The condition occurs within the first six months of life, more often in the upper than in the lower limb. It is discovered that the infant does not move one of

Pseudo-paralysis

its limbs properly, the so-called pseudo-paralysis developing, because the limb in the region of one of the bone ends is painful and swollen. In some cases the epiphysis may at a very early date become separated from the shaft and then displaced.

Morbid changes

The change is a diffuse gummatous infiltration of the cartilage and the adjacent formed bone, which breaks down into a greenish yellow fluid and thus permits separation of the epiphysis. X-ray examination is uncertain, as the epiphysis may not have begun to ossify, but it may show a diffuse osteo-periostitis.

Differential diagnosis

The differential diagnosis is chiefly from scurvy. Tuberculous arthritis must be considered, but it is more usually seen a little later in life. The absence of haemorrhages from the gums or elsewhere should suggest a syphilitic origin, and a positive Wassermann reaction will settle the problem. In scurvy, if it has existed for any time, the radiograph shows the periosteum raised from the bone with slight ossification in connexion with this membrane.

The absence of any signs of acute illness will differentiate syphilitic epiphysitis from an acute infective osteitis.

If the epiphysis has been separated the possibility of a fracture must be considered.

Treatment

The usual remedies for syphilis rapidly produce a cure of the local lesion; but the affected limb should at the same time be splinted to rest the bone.

3.—OSTEOCHONDRITIS

436.] Osteochondritis is a non-inflammatory interference with the normal process of bone growth and development, resulting in irregularity of the epiphysial junction with subsequent sclerosis. The condition may develop in almost any epiphysis, but is more common in some than in others. Its recognition is the outcome of the knowledge of bone development brought about by X-ray investigation. The symptoms are in most cases

Aetiology

due to interference with the function of some joint. The aetiology is quite unknown but among hypotheses that have been advanced are that it is due to infection, to trauma, or to abnormality of bone growth. No evidence of real value has been submitted in support of these

views. Very little is known about its pathology, because it does not prove fatal.

Osteochondritis dissecans, which occurs in the lower end of the femur *Osteo-* and in the head of the second metatarsal, is a different clinical condition *chondritis* with a very definite history of injury. It is described under the title JOINTS, DISEASES AND DISORDERS.

(1)—Pseudo-Coxalgia

Pseudo-coxalgia or Perthes's disease, the best-known example of *Perthes's* osteochondritis, develops in the upper femoral epiphysis. It occurs *disease* more commonly in boys than in girls, and at the ages of five to ten years, though examples are occasionally seen at a slightly later age. One or both hips may be affected, often one some time before the other.

The child is observed by the parents to have developed a limp, with *Signs and* which pain is seldom associated. The child is always quite fit and the *symptoms* onset does not appear to be in any way connected with previous illness.

Examination shows that there is very nearly full flexion of the hip-joint; rotation may or may not be limited, but abduction in flexion at 90'' is nearly or entirely absent. This is an almost diagnostic sign, for in no other condition of the hip-joint is free flexion associated with complete loss of abduction. Muscular spasm is not obvious as it is in a tuberculous arthritis.

On palpation the trochanter may appear more prominent than on the other side, and a fullness may be felt in the femoral triangle over the head of the femur. There is no muscular wasting or shortening of the *Trendelen-* limb, but Trendelenburg's sign is positive, showing a disturbance of *burg's sign* the mechanics of the hip-joint. This sign is demonstrated by getting the child to stand upon the affected limb with the other hip flexed to 90'', when the buttock upon the sound side is seen to drop to a lower level than the buttock of the limb upon which the child is standing.

The X-ray appearances (see Fig. 14) vary greatly with the stage at *X-ray* which the child is brought for examination. In the early stage the X-rays *appearances* do not show any of the classical changes. All that can be seen is a slight widening of the joint space compared with that of the unaffected hip. This, in association with the clinical signs, should be sufficient to enable the diagnosis to be made. In the later stages the X-rays may show fragmentation of the head with flattening, mushroom deformity, or even thickening of the femoral neck.

The prognosis depends entirely upon the time when adequate treat- *Prognosis* ment is started. If this is carried out efficiently and at an early stage, the child will recover and be left with a hip-joint which is clinically normal in every respect. The interesting feature is that early treatment, although it gives a good functional result, does not prevent the changes in the head and neck of the femur from going through their cycle. It limits, however, very considerably the severity of these changes, and hence the child is left with a good functional hip-joint. A certain degree of thickening of the neck and flattening of the head always results.

Differential diagnosis   The differential diagnosis is not very difficult. The condition is only likely to be mistaken for tuberculous arthritis or for separation of the upper femoral epiphysis. In tuberculous arthritis, however, the age of incidence is rather later and movement is limited in all directions. Flexion of the hip-joint in pseudo-coxalgia is almost full, but abduction of the thigh with the hip flexed to 45 is either completely or almost completely absent. This is a most important diagnostic sign. In addition the child is healthy. Limitation of abduction is present in both a pseudo-coxalgia and separation of the femoral epiphysis, but in the latter condition there is complete loss of internal rotation with more muscular
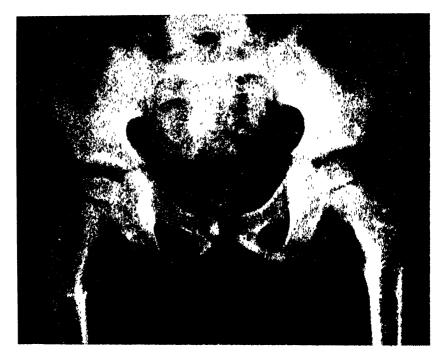
Fig. 14.—Early pseudo-coxalgia

spasm and slight shortening, and the trochanter is raised above Nélaton's line. The radiological appearances are quite different.

Treatment   Treatment consists in complete relief from weight-bearing of any kind until the X-rays show that the head of the femur has been restored to its normal density. As already stated, the head may be a little flattened and the neck thickened, but the surface of the head is smooth and fits the acetabulum, unless the condition was very far advanced when treatment began. It may be necessary to maintain relief from weight-bearing for eighteen months. Treatment of a child with pseudo-coxalgia in a walking calliper is in view of present knowledge quite inadequate; the best method is to fix the child upon a Robert Jones' abduction splint, an easy procedure once the details have been mastered. After the necessary period of relief from weight-bearing has passed no other form of splintage or treatment is required.

(2)—Köhler's Disease of the Tarsal Scaphoid

This is an osteochondritis which develops in children between the ages of three and six years. The child complains of a little pain in the foot and begins to limp or turn its foot inwards. Upon clinical examination the foot may appear a little swollen over the inner border and this area will be tender, but an abscess never develops; the presence of an abscess would be evidence that the lesion was tuberculous.

X-ray examination shows an interference in the ossification of the scaphoid. The bony nucleus is thinner, denser, and perhaps fragmented. *X-ray examination* The differential diagnosis from a tuberculous osteitis is perhaps difficult on clinical signs, but in the latter the X-ray examination shows that the bony nucleus of the scaphoid is irregular and not fragmented, and that the other bones of the tarsus are somewhat atrophic.

The treatment consists in strapping the foot, or, if this makes the *Treatment* condition more painful, fixation in plaster for a month. The symptoms subside very rapidly and a normal foot results without the necessity of providing relief from weight-bearing.

(3)—Apophysitis of the Calcaneus (Osgood's Disease)

This is osteochondritis of the cap-like epiphysis on the posterior aspect of the calcaneus (os calcis). The child complains of pain and tenderness in the posterior or under surface of the heel. It usually comes on without any obvious reason, though a history of injury may in some instances be obtained. X-rays show increased density and fragmentation of the epiphysis. The symptoms last for a variable period and subside without any active treatment except elevation of the heel of the shoe to diminish the strain of the tendo Achillis on the epiphysis.

(4)—Osgood-Schlatter Disease

Described originally in 1903 by Osgood, this condition of osteochondritis affecting the upper tibial epiphysis is now well recognized. It is most common in boys of school age. The portion of the tibial epiphysis affected is the tongue-like protrusion which lies over the anterior aspect of the shaft; it may be partially separated and lifted forwards and is also fragmented.

The early symptoms are slight and consist of aching or pain over the *Signs and* front of the leg after exercise; the area is tender on pressure, thickened, *symptoms* and perhaps swollen, and there may be inability fully to extend the knee-joint. If unilateral the condition is quite obvious by comparison with the other side. The diagnosis is easy and seldom gives rise to any trouble.

Treatment consists in strapping the limb to relieve tension of the *Treatment* patellar tendon so that when the limb is extended it does not pull so hard on the epiphysis. At the same time all strenuous games or long walks must be given up until symptoms have completely subsided. In a very few patients this treatment does not relieve symptoms and the knee must be fixed in plaster or a knee-cage. Even after all symptoms

have subsided and the function of the limb is normal, a certain amount of permanent thickening persists.

(5)—Vertebral Epiphysitis: Adolescent Kyphosis

This condition, which seldom gives rise to any symptoms except an occasional backache, develops gradually, chiefly in boys about 15 years of age. The patient stoops badly, carrying the head forwards with the shoulders drooping. Clinical examination reveals only a gradual kyphosis which is free from any signs and cannot be corrected.

X-ray examination The lateral radiograph of the spine shows that the vertebral bodies are wedged, the epiphyses irregular, and the intervertebral discs narrowed. Prolapse of the nucleus pulposus of the intervertebral discs may be present and produce notches in the bodies of the vertebrae.

Treatment In the early stages the boy must be treated in recumbency on a frame or plaster bed. This will prevent the condition from progressing and may straigthen out what deformity has already developed. When the condition is cured, as shown by X-rays, the child may be taken off the frame and given exercises for the muscles of the back. A Jones' back-brace, which should be worn for at least six months, is provided when the upright position is resumed. When an adolescent kyphosis has become really rigid it is waste of time to attempt to correct it.

4.—NEW GROWTHS

437.] Malignant growths are never primary in the epiphysis though they may invade it from without; it may, however, be the site of non-malignant growths, i.e. chondromas, cancellous osteomas, and benign giant-cell tumours.

Chondroma Chondromas, lobulated, encapsulated tumours, grow slowly from the cartilaginous elements of the developing bone. They may become partly calcified in the centre but true ossification never occurs. The tumours may be single or multiple, the latter occurring most commonly in the hands and fingers.

Treatment The cartilaginous tumour can be removed, and should the affected bone be severely damaged in the process it can if necessary be strengthened by a bone graft.

Exostosis Exostosis or cancellous osteoma arises from the epiphysial cartilage. It is composed of a layer of compact bone enclosing cancellous tissue and covered with a cap of cartilage. As a rule it is pedunculated, the pedicle sometimes being of considerable length. With the growth of the bone the exostosis becomes situated further and further away from the epiphysis; when this growth ceases, that of the exostosis does too. The commonest site is the lower end of the femur or the upper end of the tibia. Symptoms occur only when an adventitious bursa develops over the exostosis or when the surrounding structures are interfered with by its presence.

Benign giant-cell tumour, or osteoclastoma, in contrast to the osteo- *Osteo-*
genic sarcoma which develops in the metaphysis close to the epiphysial *clastoma*
cartilage, is a tumour of the epiphysis. It starts in the cancellous tissue
and develops eccentrically, so that in time the epiphysis may be largely
destroyed. This tumour does not invade the surrounding structures but
may reach a large size before attention is drawn to its presence. Like
exostosis, it is seen most often in the upper end of the tibia or the lower
end of the femur.

The symptoms are pain and perhaps tenderness, with later swelling. *Symptoms*
Occasionally the first evidence of the tumour is the occurrence of a
pathological fracture.

The X-ray appearance is characteristic. The affected bone is enlarged *X-ray*
and occupied by a cystic trabeculated swelling. The separation between *appearance*
the tumour and normal bone is sharply defined. The giant-cell tumour
is in direct contact with the articular cartilage though it does not
destroy it.

Thorough curettage is usually successful in removal of the tumour, *Treatment*
though a certain number of recurrences occur. The recurrences are said
to grow more rapidly than the primary tumour and even to become
malignant. If the tumour when first recognized is very extensive, the
limb may have to be amputated for the sole reason that it cannot be
strengthened sufficiently after the tumour has been curetted out. Deep
X-ray therapy or radium is now used extensively in place of operation
with promising results.

5.–INJURIES: SEPARATION OR DISPLACEMENT

438.] Fracture may occur in any epiphysis but, except in the lower epi-
physis of the humerus, is extremely rare. On the other hand separation
or displacement of the epiphysis from the shaft of a bone is common,
and in certain situations occurs where in the adult there would be a
fracture of the bone. The reason for this is obvious: the epiphysis is
joined to the shaft by the epiphysial cartilage in contact with which is
the newly formed bone, the result of ossification of the cartilage. This
newly formed bone is not so strong as that further down the shaft and
is liable to fracture with injury.

Most separations of epiphyses are strictly speaking fractures through
the metaphysis and, when a separation or displacement occurs, the
epiphysis is always displaced with a small fragment of the metaphysis
attached to it.

At the time of displacement there is a great risk that the epiphysial *Injury to*
cartilage may be damaged, in which event growth of the bone may *epiphysial*
become irregular or even cease altogether. This occurs with sufficient *cartilage*
frequency to be recognized as an important sequel of any accident. *Comparison*
The situation in which a separation of the epiphysis takes place is *of upper*
important as regards the future development of the bone, because *and lower*
epiphyses

increase in length of a bone is greater at one end than the other, thus if the lower epiphysis of the femur is separated and early union takes place, the interference with growth will be much greater than if the upper epiphysis had been separated.

Separation is much commoner in some epiphyses than in others. The displacement of the epiphyses is always in the same direction, because the responsible force always acts in the same way.

All displacements of the epiphyses are very difficult to reduce, but once reduced do not tend to recur.

(1)—Separation of Epiphyses of Humerus

(a) *Lower Epiphysis*

Incidence   This, probably the most common separation of the epiphyses, occurs in children between 7 and 12 years of age, seldom younger or older.

Causes   The usual accident is falling off a gate or fence. The degree of separa-
Degree of displacement   tion or displacement varies greatly; in some cases the epiphysis is only separated, in others it may be taken completely off the shaft and displaced backwards and upwards, together with a fragment of the shaft. In addition to this displacement, the epiphysis is also displaced either inwards or outwards, according as the forearm is adducted or abducted at the time of the accident.

Diagnosis   Separation with displacement of the lower epiphysis can usually be diagnosed easily if seen soon after the accident. It is only likely to be mistaken for a dislocation of the elbow-joint, which occurs more often in adults than in children. If there is much swelling it may be difficult to be sure what has happened, but this state of affairs always suggests fracture. Simple separation of the epiphysis without displacement does not give rise to so much swelling. When the separation is complicated by fracture it may be very difficult to secure restoration of function.

X-rays will reveal the degree of displacement and the position of the
Complications   fragments. In addition to the bone injury this accident is very often complicated by injury to the surrounding soft structures, but important vessels or nerves are seldom injured.

Treatment   Under full anaesthesia the forearm should be pulled upon and the lower fragment completely disimpacted, for if this is not done a satisfactory reduction cannot be obtained. To move the lower fragment forward again, the forearm is hyperextended while extension is being applied. As the result of hyperextending the forearm the olecranon fits into the hollow in the back of the epiphysis and can be used to lift the epiphysis forwards. If the fragment can be moved forwards it will usually be found that any lateral displacement will be easily corrected. Except in isolated parts of the country this fracture should always be reduced on an X-ray table and a film taken at once, so that if reduction has not been satisfactory further correction can be attempted. After such manipulation has been completed and the reduction is seen to be satisfactory, the forearm should be slung with a collar and cuff in as much flexion as the swelling around the elbow will permit. It is quite

unnecessary, and is indeed dangerous, to get full flexion. Movement at the elbow-joint will always return if the displacement has been reduced properly, though this may take as long as twelve months.

If reduction cannot be obtained satisfactorily by manipulation it will always be a question whether or not open operation is desirable. Open operation is difficult and after it a great many elbows become stiff. Often an incomplete reduction gives a better functional result than does a perfect anatomical reposition.

The after-treatment of this injury is simple and can be summed up *After-care* briefly. The patient should be allowed to move the joint actively as much as he wishes, and function will be rapidly restored. Neither massage nor physical treatment of any kind should be given for it only does harm. Myositis ossificans never develops with active movements but more often than not it does so with passive movements.

Nerve injuries in association with separation of the lower humeral epiphysis are generally only transitory.

Volkmann's ischaemia, the most troublesome complication which *Volkmann's* can follow separation of the lower humeral epiphysis, generally develops *ischaemia as a* because a satisfactory reduction of the fracture has not been effected. *complication* It may result from severe damage to the blood-supply of the muscles at the time of the accident, in which case it may be inevitable. It can usually be avoided by proper reduction of the fracture without any attempt to fix the elbow in too much flexion. Any bandage around the elbow after this injury is a source of danger, for if the limb swells it may constrict the vessels.

(b) Upper Epiphysis

Separation of the upper epiphysis of the humerus is rare and restoration of position is difficult. Even if the injury is left unreduced permanent disability does not result.

(2)—Fracture of Capitellum

Fracture of the capitellum, a not uncommon injury to the lower humeral epiphysis, is usually associated with marked rotation and outward displacement of the fragment. Manipulation if tried early may succeed in reducing it, but more often the fragment is so much rotated that it must be turned round and replaced by open operation. Once reduced into position it does not tend to slip out again, because the head of the radius keeps it in position. The elbow, however, should be splinted with a posterior plaster slab for about a fortnight. Restoration of function is complete.

(3)—Separation of Internal Epicondyle

This is probably nearly as common as separation of the lower epiphysis *Causes* of the humerus. It is due to the action of an abduction force to the forearm, which pulls off the epiphysis, displacing the fragment downwards with the common origin of the attached flexor muscles. If the

abduction force is severe it may open out the inner side of the elbow-joint, and the fragment may become caught in the joint. This injury occurs also with outward dislocations of the elbow joint, and when the dislocation is reduced the epiphysis may be caught.

Treatment

If the displacement of the fragment is only slight the forearm should be kept in a sling until the symptoms subside. When the fragment is much displaced or caught in the elbow-joint, it must be freed and then fixed in position either with catgut sutures or a bone peg.

Resulting injury to ulnar nerve

The ulnar nerve is very often bruised or pressed upon in this injury, or it may be stretched, afterwards giving rise to what is known as a late ulnar palsy. For this reason if the internal epicondyle must be fixed in position by open operation it is wise at the same time to transpose the ulnar nerve to the front of the condyle.

(4)—Separation of Lower Epiphysis of Radius

Causes

This injury, like a Colles's fracture, results from falling upon the outstretched hand. It may be a simple separation without any displacement, but more often the epiphysis is displaced backwards with a portion of the posterior part of the shaft attached.

Treatment

Such a displacement may be very difficult to reduce and a good deal of force, even the use of a Thomas's wrench, is often necessary. Unless the epiphysis is restored to position the inferior radio-ulnar joint is interfered with. Fixation in plaster for about four weeks is necessary.

Sequelae

The only complication that occurs arises from early union of the epiphysis with the shaft, for if the separation takes place at an early age the ulna, by reason of its continuous growth, becomes subluxated backwards and weakness of the wrist develops.

(5)—Separation of Upper Epiphysis of Femur

In the lower limb the upper epiphysis of the femur is separated more commonly than any other. Thirty years ago the lower epiphysis of the femur was the more often affected, but with the passing of the horse carriage this accident has become very rare.

Causes

The upper epiphysis of the femur may undergo separation and displacement in certain conditions of bone softening, but traumatic separation may be either sudden or gradual. A common history in gradual separation is that a boy, while playing football or cricket, experiences pain in the hip, which is not so severe as to make him complain. About ten days later he may be seized with sudden pain in the hip and be unable to walk or only able to do so with a limp.

Signs and symptoms

Examination shows limitation of movement in the affected hip, especially of abduction and internal rotation, the hip being often fixed in adduction and external rotation. There may be about half an inch of shortening and the trochanter is slightly raised. A variable amount of muscular spasm is present.

Diagnosis

The differential diagnosis is very easy, for in a child or young adolescent no other condition produces the clinical signs of limitation of abduction

and internal rotation with pain and spasm. It is quite unlike either a tuberculous hip or pseudo-coxalgia.

The treatment consists in recumbency in bed with skeletal traction *Treatment* applied to the upper end of the tibia. A weight up to 30 pounds is necessary to reduce the displacement of the neck and bring it back into position with the head. Once the position has been restored the weight can be reduced to 8 or 10 pounds. If the extension is applied to the tibia it is found that internal rotation is automatically restored. The child must be kept in bed for about ten weeks and may then safely begin to bear weight on the limb again. No calliper is needed as the separation does not recur after a suitable interval.

Should the patient not be seen until some weeks after the separation, no attempt should be made by open operation to restore the separated epiphysis. This is certain to make the hip-joint stiff and may result in an aseptic absorption of the head of the femur. Union should be allowed to take place in the position the bone has taken up, and then at a later date a subtrochanteric osteotomy should be performed to correct the external rotation and adduction deformity; this treatment will result in a hip-joint with nearly perfect function. When early union of the epiphysis occurs, shortening of the limb develops and may in the end be as much as one and a half inches, depending upon the age of the child at the time of the accident.

(6)—Separation of Lower Epiphysis of Femur

This now very rare injury is the result of a hyperextension of the limb, *Cause* the epiphysis being displaced forwards so that the fractured surface lies on the anterior aspect of the end of the shaft. At the time of the accident severe injury may be done to the vessels in the popliteal space, which may necessitate an amputation of the limb. If the damage to the soft structures is not of importance the epiphysis can be restored to its position.

If the patient is seen soon after the accident, when he has recovered *Treatment* from the shock, it may be possible under an anaesthetic to reduce the displacement by traction on the limb, flexion of the knee, and, if this fails, manipulation.

Traction is applied by means of a pin through the upper end of the tibia and, in the course of a few days, the epiphysis will gradually slide down over the end of the shaft, where it will be restored to its normal position and later join on again.

There is a very grave risk that the epiphysial cartilage may be damaged, as it is in most of these injuries, and if it is, the whole, or part on the inner or outer side, of the epiphysis may unite with the shaft. If the epiphysis is replaced by open operation—a procedure which may sometimes be necessary—it will certainly join at once, and if complete fusion occurs a great deal of shortening will result, even as much as six inches, depending again upon the age at the time of the accident.

With partial union either genu varum or genu valgum develops. Under

these conditions the undamaged portion of the epiphysial cartilage must be destroyed at the time of the osteotomy to correct the existing deformity, which otherwise will only recur.

(7)—Separation of Lower Epiphysis of Tibia

Separation of this epiphysis with displacement outwards is not uncommon. It may or may not be associated with a fracture of the fibula. It is the Pott's fracture of the child, the result of an abduction injury. The separation is easily reduced and the limb is fixed in plaster for six weeks.

Resulting deformity

Here again partial union of the epiphysis results in the development of an adducted and inverted foot, the epiphysis on the inner side of the tibia ceasing to grow while that on the outer side continues to do so. The fibula likewise continues to grow, pushing the foot more and more over.

Treatment of deformity

Treatment of this deformity is to correct the alignment of the ankle-joint by an osteotomy of the tibia, at the same time removing the lower epiphysis of the fibula with sufficient bone above to permit the foot to be easily held in the corrected position. The limb is afterwards fixed in plaster until firm union has taken place.

(8)—Separation of Other Epiphyses

The epiphyses of the other bones seldom separate, and if they do so treatment is carried out on similar lines.

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EPISPADIAS

See UROGENITAL ORGANS, ABNORMALITIES

EPISTAXIS

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Reference may also be made to the following titles:

HAEMOPHILIA   HAEMORRHAGIC DISEASES
NOSE DISEASES

1.–AETIOLOGY

439.] Bleeding from the nose is most commonly due to a local condition but sometimes to a general disorder, and the presence of a local cause does not preclude the existence of a general disorder in the background. It is common in children and in elderly persons but rare in infancy. Headache and tinnitus sometimes precede an attack.

Local causes The local causes may be injury, rhinitis sicca with crusting, adenoids, tumours—including both innocent and malignant, and bleeding polypus of the septum—and ulceration due to syphilis, tuberculosis, caries, or foreign bodies.

By far the commonest local cause is a varicose condition of the veins in the anterior part of the septum, often associated with a superficial erosion caused by rhinitis sicca. This haemorrhage is usually regarded as arterial and as arising from the 'artery of epistaxis', which lies just under the mucous membrane of the nasal septum about a quarter of an inch inside the vestibule and a quarter of an inch above the floor of the nose. This spot from which the bleeding usually starts is sometimes called the area of Kiesselbach or of Little, but it is evident from clinical observation that the haemorrhage is usually venous, and that often there is not merely a bleeding point but an intensely congested bleeding

area. In other cases the bleeding is arterial and comes from an opening in the side of a vessel which at once ceases to bleed when it is cut across with a cautery. An uncommon but interesting cause of epistaxis was described by Osler, who pointed out that repeated epistaxis from angiomas on the septum is a prominent symptom in multiple hereditary telangiectases (see also p. 148).

Numerous general conditions predispose to epistaxis. Among these are: arteriosclerosis and chronic interstitial nephritis; chronic bronchitis and emphysema; mitral disease; whooping cough; hepatic cirrhosis; the acute specific fevers, especially enteric fever and influenza; and disorders of the blood, especially haemophilia, purpura, scurvy, and the leukaemias. High altitudes and tropical heat are also common causes. *General predisposing conditions*

On examination of the nose the bleeding spot will usually be found at the site of predilection already mentioned, if there is no gross lesion causing it; but it sometimes arises from the floor of the nose, from the anterior end of the inferior nasal concha (inferior turbinal), from veins much further back on the septum, or from anterior ethmoidal veins high up in the nose. *Sites of bleeding*

2.–DIAGNOSIS AND PROGNOSIS

In forming a diagnosis and thereby making a prognosis the general state of the patient must be investigated, especially the arterial tension and the temperature. The onset of influenza or enteric fever and the existence of a blood disease or of a gross injury such as fracture of the anterior fossa must be excluded. Locally it is important to exclude a malignant tumour of the ethmoidal region, as repeated epistaxis may be the first symptom of this. The same is true of nasopharyngeal fibroma, a rare tumour which occurs only in young males between the ages of fifteen and twenty-five.

Apart from underlying causes the prognosis is rarely serious, but occasionally the bleeding comes from a large area of degenerated mucous membrane and is only arrested with great difficulty by removing a large part of the septum with its covering of mucous membrane. Parker recorded such a case. *Prognosis*

3.–TREATMENT

In most cases epistaxis ceases spontaneously; but when this does not happen, the bleeding spot should be located and the vessel obliterated with the electric cautery. It often happens that when the nose is examined it is found that the bleeding has ceased for the moment. A touch with a probe will then start it again and indicate the spot from which it comes. A small piece of cotton-wool soaked in 10 per cent solution of cocaine hydrochloride is then applied firmly to the bleeding spot with forceps. *Cocaine*

This arrests the bleeding and renders the mucous membrane anaesthetic.

Cauterization   If the haemorrhage is arterial from a small branch of the spheno-palatine artery, the artery is cut across with the cautery and sealed, and the bleeding ceases at once. If the bleeding is venous from a velvety vascular area it is not arrested quite so easily, because the edges of the cauterized area may continue to bleed. It is thus sometimes necessary to cauterize an area of five millimetres or even more in diameter until the edges cease to bleed. The cautery should be applied very lightly at the edges and the current should not be cut off while the cautery point is still in contact with the tissues, otherwise the point adheres and the withdrawal may start the bleeding afresh. An oily spray should be used for the nose afterwards; one containing chlorbutol 1 per cent with menthol and camphor in light liquid paraffin, as in chloretone inhalant, is suitable.

Packing the nasopharynx   Packing the nasopharynx and such devices as rubber bags which can be inflated and so exert pressure are unnecessary; but if the cautery is not available or the bleeding spot cannot be treated, the nose may be packed with ribbon gauze moistened with adrenaline hydrochloride solution diluted with physiological saline to 1 in 10,000. The best way to apply this packing is to take a strip of ribbon gauze half an inch wide and eighteen inches long and to tie silk threads to it at intervals of four inches. As the nose is packed with angular nasal forceps aided by a speculum and good illumination, the silk threads can be used to exert counter-pressure, and so the nasal fossa is packed firmly. The packing should never be left in place for more than twenty-four hours, as it becomes infected and may cause otitis media or other local septic infections by interfering with the drainage from the nose.

Viper venom   It is possible that in troublesome cases of epistaxis, associated with disorders of the blood, the recently introduced method of applying a solution of venom of Russell's viper may prove useful, as solution of 1 in 10,000 of this preparation appears to cause immediate clotting in all circumstances; Higgins and Thorne reported such a case. Blood transfusion might be indicated in exceptional conditions.

Treatment of angiomas and polypi   Angiomas are better treated by electrolysis than by application of the cautery. In bleeding polypus of the septum, an innocent fibro-angioma, it is better to remove the tumour with its base of mucous membrane under cocaine and adrenaline anaesthesia than to attempt to destroy it with the cautery, which is difficult.

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EPULIS

See MOUTH DISEASES

ERGOTISM

See ARTERIAL DISEASE AND DEGENERATION, Vol. II, p. 43

ERUPTIONS, ANOMALOUS AND ATYPICAL

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1.—GENERAL SURVEY

440.] This article is intended to aid the practitioner in the diagnosis of eruptions which either do not correspond with the usual descriptions or do not readily fall under the headings of usual nomenclature. In some instances the difficulty is attributable to the fact that the disease, although common, is accompanied by unusual features. In others the signs are the result of some treatment, article of diet, or occupation, that

the patient does not associate with them and therefore does not think worth mentioning. In others again the syndrome, though already described and named, is not sufficiently well known to have obtained a place in the common nomenclature.

Such an article must necessarily be disjointed, for it consists of a list of instances that have presented difficulty after years of practice and still do so. Nevertheless an attempt has been made to arrange these examples in some kind of order.

2.–ALTERATIONS IN THE COLOUR OF THE SKIN

(a) Punctate pigmentation of the skin of the face and trunk.   *Punctate*

Patients occasionally complain of punctate blackening of the skin. *pigmentation* On examination the discoloration is found to lie almost exclusively at the mouths of the sebaceous follicles and sweat glands. Not uncommonly the patient states that the trouble began with heat and redness. Actually what has happened may be that the patient, having suffered from some slight irritation of the face, has used sulphur ointment, which is a favourite lay remedy. Not improving, or more probably getting worse, *Causes* she then consults her doctor without telling him what she has done. He prescribes a lead lotion which results in the formation of black sulphide of lead in the pores. The discoloration may also occur without the previous use of sulphur externally if the patient has been ingesting it, and it may also occur, though much more rarely, if the patient naturally excretes some sulphur by the skin without taking it. This form of discoloration is not confined to cases in which an application containing lead has been used, but may be the result of the application of a powder containing a bismuth salt to a skin which is carrying sulphur.

(b) Patches of pigmentation of irregular shape, usually situated below *Berlocque* or behind the ears or on the interclavicular notch.   *dermatitis*

These may be due to the application of perfume and form the so-called 'perfume' or 'berlocque' dermatitis (see Vol. II, p. 713, and Vol. III, p. 613).

(c) Irregular patches of pigmentation usually situated on the forehead *Chloasma* or temple in women (chloasma uterinum).   *uterinum*

These are found not uncommonly during pregnancy and usually fade after the birth of the child, but may also occur at the menopause, in which case they are usually permanent. The cause is unknown, but they may be the result of some endocrine imbalance. When occurring in adult women but in neither of the above-mentioned circumstances they call for a thorough examination of the pelvic organs.

Treatment of these patches is not very satisfactory, but they may *Treatment* sometimes be made to disappear by painting them with a solution containing 2 per cent of acetic acid and 0·1 per cent mercuric chloride in alcohol.

Pigmentation of eyelids

(d) Pigmentation of the eyelids, especially if associated with darkening of the ocular conjunctiva, should always suggest localized argyria as the result of the application of silver salts to the eye. In cases of general pigmentation without apparent cause the possibility of argyria due to the ingestion of silver must be borne in mind, though this is now rare.

3.—ALTERATIONS IN THE VESSELS

Familial haemorrhagic telangiectasia

(a) Familial haemorrhagic telangiectasia (Osler-Weber syndrome).

This somewhat uncommon disease has been known for a long time, but unfortunately the earlier observers confounded it with haemophilia owing to its frequent association with persistent and even dangerous haemorrhage.

Historical

In the earliest description that I have seen Wickham Legg (1876) reported cases in a man aged 62, his sister, daughter, and son. In the light of modern investigation this group belonged unquestionably to the disease here described. Osler again called attention to the disease in 1901 and in 1907, and since that time fresh groups have been recorded, but not much has been added that is new.

Morbid anatomy

Schuster (1937), however, reported a case in which exhaustive post-mortem examination was performed, the following defects being found: telangiectases in the larynx, trachea, stomach, and intestines. Dilated veins were also found beneath the capsule of the liver, and doubtful haemangiomas in the upper lobe of the right lung. The spleen was large and soft, and there were three aneurysms of the splenic artery.

Twenty fatal cases have been recorded, mostly from anaemia, but in two cases gastric carcinoma has been found. Microscopic examination of the lesions suggests the formation of new vessels.

Aetiology

The disease has been generally noted in adults who have often given a history of epistaxis in early youth, and it would therefore appear that it is progressive, especially in its tendency to affect the skin (see also p. 143).

Clinical picture

The patient generally seeks assistance on account of the bleeding, which is usually from the nose. The skin and mucous membrane of the nose are beset with dilated vessels from one of which the haemorrhage arises. Examination then reveals the presence of telangiectases elsewhere. The chief sites in which they are found are the lips and buccal mucous membrane, the face, and the trunk, but in Schuster's case they were present also on the palmar aspects of the fingers.

Three forms are found, namely, small red dots the size of a pin's point, spider telangiectases which are the most common, and small nodular angiomas. It would seem that if the disease is known to the observer, mistakes in diagnosis will be unlikely.

Anaemia as sequel

Post-haemorrhagic anaemia is a common result of the repeated haemorrhage, and patients may present themselves for treatment on account of debility.

(b) Progressive angiomas of pregnancy.

These are very rare tumours but so striking that they deserve a short description. They occur on the face in the early months of pregnancy and continue to enlarge during its course.

I have seen one on the muco-cutaneous margin of the upper lip which enlarged to the size of a green pea and was very disfiguring. Freezing with solid carbon dioxide was of no avail, but the growth shrank in a few weeks after the birth of the child, leaving only a minute red dot which was easily obliterated with a single puncture by the electrolytic needle. Gans figured a section of one from the cheek of a girl two months pregnant but apparently did not connect it causally.

The chief reason for describing this curious growth is that it naturally distresses the bearer who can with satisfaction be assured that it will disappear after labour.

(c) Large patches of telangiectases associated with obvious or barely perceptible cutaneous atrophy.

These cases are less common than they were and are generally due to previous exposure to X-rays. The patches usually appear on the abdomen or lumbar region and are a sequel to prolonged exposure of the abdomen to X-rays. As they come on years after the exposure, the patient does not connect them with the treatment and therefore may not mention it. Such patches usually itch. (See also Vol. III, p. 611.)

4.–ERYTHEMATOUS LESIONS

(a) Erythematous patches and streaks of unusual shape, generally situated on the proximal parts of the limbs and trunk, of short duration and sometimes going on to vesiculation.

These may be mistaken for a 'feigned eruption' but are in reality accidentally produced by the contact of plants, combined with sunlight during sunbathing. Probably more than one plant may be responsible; at any rate it is not definitely known which. The eruption may go on to vesiculation in some cases and is known as 'meadow dermatitis' (see Vol. III, p. 613).

(b) Persistent erythema on one cheek of a child.

This may cause great anxiety to the mother. It is apparently due to the irritation of an erupting molar and subsides when the tooth is fully developed. On rare occasions herpetiform vesicles may form on the patch.

(c) Persistent redness with gradual thickening of the skin over the cartilaginous portion of the nose.

This is merely an exaggeration of what occurs in most people in old age. If it occurs in any marked degree below the age of sixty it is generally a sign of myocardial degeneration. It is a cause of much distress to some patients, who may come for advice for this symptom alone.

Erythema due to antral disease

(d) Recurrent or persistent erythema of one cheek often associated with some swelling of the lower eyelid and sometimes conjunctivitis.

I have seen a fair number of these patients, who generally attributed the condition to gout because it was associated with pain in the joints and elsewhere, but in all my cases it proved to be due to antral disease.

5.–URTICATE LESIONS

Bites of bed bugs

(a) One or more groups of large urticarial papules often arranged lineally.

This should always arouse the suspicion of the presence of a bed bug. The reasons for mentioning this are the extraordinary difficulty of finding the insect and the rooted objection of a cleanly patient to admit its possibility. (See also BITES AND STINGS, Vol. II, p. 346.)

Pediculosis capitis

(b) Sparsely scattered small urticarial lesions on the root of the neck and the shoulders posteriorly.

This should always evoke a very careful search for pediculosis capitis. It is not sufficiently known that the head louse (*Pediculus humanus capitis*) and the body louse (*P. humanus corporis*) are varieties of the same species (*P. humanus*). Normally their habits are different, but if the head louse falls from the hairy scalp it may bite anywhere.

Leprosy

(c) Persistent, urticate, large papules on the forearms associated with a rather burning itching and tingling in the tips of the fingers.

This combination is in my experience rare. The patient should be asked if he has lived long abroad and the possibility of early leprosy should be investigated.

6.–ITCHING WITHOUT OBVIOUS SIGNS

General pruritus

(a) General itching in people who have lived long in the moister tropical regions, especially the East Indies.

On examination the skin may be found to be drier than that of the average person. An occasional Turkish bath sometimes helps these people, as does the gentle rubbing in of glycerin 5 per cent in water. Baths should be few in number and short in duration. Soap should be avoided.

Associated with abdominal carcinoma

(b) Itching without any sign of cutaneous disturbance in elderly people, generally confined to the lower thorax and abdomen.

A thorough examination of the abdomen should be made, as this condition is occasionally associated with abdominal carcinoma, especially of the liver.

Associated with scabies and pediculosis pubis

(c) Itching associated with an eruption that would otherwise be diagnosed as syphilis.

It may perhaps be pointed out that syphilitic eruptions of the scalp and scrotum not infrequently itch, thus forming an exception to the rule that syphilitic eruptions do not do so. In the case of eruptions in other parts which appear to be syphilitic but are associated with itching,

a careful search should be made for an accompanying parasitic eruption such as scabies or pediculosis pubis.

7.–SCALING AND PAPULAR ERUPTIONS

(a) Discs or circles of papulo-squamous eruption on the forearms with *Scabies* little eruption elsewhere.

These are apt to be mistaken for 'seborrhoeic' eczema, but very rarely, if ever, are seborrhoeic eruptions found on the forearms in the absence of the disease on the trunk. In all such cases scabies should be suspected, and a careful search should be made for the burrow. In clean people there is often very little to be seen on the hands, but close examination with a lens may reveal the characteristic burrow, which will be white instead of black and therefore easily overlooked. (See also SKIN ERUPTIONS DUE TO INSECTS AND ACARINES).

(b) A miliary eruption of very small papules on the trunk especially *Molluscum contagiosum* affecting the shoulders.

On rare occasions patients come for treatment after unsuccessful treatment for seborrhoeic eczema. The condition may be a curious form of molluscum contagiosum in which the lesions are unusually numerous but none of them large enough to be easily diagnosed. In such cases there is severe itching, and this feature increases the probability of confusion with eczema. (See also SKIN TUMOURS.)

(c) Oval or round pink patches with raised edges and scales which *Lichen planus* have their detached edges pointing towards the centre.

Such cases are almost certain to be diagnosed as pityriasis rosea, and it is only after they have persisted far beyond the duration of this disease that the mistake is recognized.

There is a peculiar type of lichen planus which on rare occasions presents this appearance. The mucous membranes should be inspected, and the general surface of the skin should be examined with oblique lighting. In some cases colourless minute lichen papules may be shown up by this method. (See also LICHEN.)

(d) Figurate scarcely raised scaly patches of the upper arms and thighs. *Dermatitis colonica* 'Dermatitis colonica.'

This curious and not very commonly recognized eruption was described and named by me in 1932 as the result of repeated bacteriological investigations. The patient, though generally in good health, may suffer from mild indigestion and looseness of the bowels, but very rarely from constipation. The eruption is in the form of very slightly scaling, oval or circular patches with a diameter of half to one inch. The loose edges of the scales point in all directions, thus distinguishing it from pityriasis rosea. There are not any raised papules, but on the margins of the patches are macules about one-sixteenth of an inch in diameter, and these show a slight degree of telangiectasis if examined with a lens. Itching may be almost completely absent or be of considerable intensity.

The disease is always aggravated by a hot bath but is uninfluenced, or more commonly even benefited, by sea-bathing; it is essentially chronic.

Alteration in colonic flora
Repeated examination of the stools by more than one bacteriologist showed that it was associated with great diminution or absence of *Bacterium coli* (*Bacillus coli communis*) and increase in the number of streptococci, which may be of any variety. The name was adopted because the condition was evidently due to an alteration of the colonic flora but was not associated with the presence of any particular pathogenic organism. It can be cured usually by appropriate dieting and the administration of internal antiseptics.

(e) Persistent scaling of the moustache area in men.

I have not seen this trouble in clean-shaven men or in women. The patient complains of persistent scurfiness in the moustache and perhaps dryness of the mucous membrane of the upper lip in addition. The condition is benefited but not cured by the application of any bland ointment. It is usually caused by the use of mouth-washes or dentifrices containing salol and disappears rapidly after they have been given up.

(f) Persistent or repeated folliculitis on the chin in women.

This condition may be mistaken for acne of the chin, a rather common affection in women of middle age. Closer inspection, however, shows that comedones are not present and that the folliculitis is irritative *Association with epilation* rather than suppurative. The lesions may be simply the result of epilation of superfluous hairs. Occasional pulling out seems to do little harm, but if the growth is strong so that epilation is often used a chronic folliculitis with thickening of the skin may result. (See also HAIR FOLLICLES, ABNORMALITIES AND DISEASES.)

8.—OVERGROWTH AND NEW GROWTH

(a) Painful keratoses of the upper rim of the ear.

Aetiology
These are often mistaken for, and called, gouty manifestations. They are in fact horny growths which develop as the result of repeated chilblains (see ANGIOKERATOMA, Vol. I, p. 576, and CHILBLAINS, Vol. III, p. 120). They are intensely painful and if bilateral may prevent the patient from sleeping on his side. They are usually found in later middle life, but I have seen them in schoolboys. Hunting and shooting men are particularly liable to them from exposure, and as these often take a generous amount of alcohol the idea that the condition may be gouty is suggested.

Treatment
The best treatment is excision by means of two almost parallel crescentic incisions to include the growth. The resulting scar is imperceptible. If excision is refused, inunction with an ointment containing 20 per cent of salicylic acid may be tried. This usually relieves by softening and removing the horny tissue, but it seldom cures.

(b) Atypical keratoses over the joints of the middle and terminal interphalangeal joints.

These are seen somewhat uncommonly at school age and more

frequently in late middle age. They should lead at once to investigation to determine whether the patient is suffering from osteoarthritis.

Allied to this condition are cystic swellings, sometimes covered by hyperkeratosis, over the terminal interphalangeal joints. These are in reality hernial projections from the joint and must be treated with great respect. If they reach sufficiently near the surface to threaten rupture they should be removed with full aseptic precautions, as they generally communicate with the joint. The content is a clear gelatinous fluid.

9.–ANOMALIES OF THE HAIR AND NAILS

(a) Patches simulating alopecia areata, sometimes occurring in apparent *Trichotillo-* epidemics in children but showing many broken hairs without the *mania* characteristic 'note of exclamation' stump.

This condition may be due to artificial epilation of the hair by a nervous child and may be imitated by his companions. If the hair is kept too short for the child to be able to pull it out, the habit may be broken. The name given to this condition is trichotillomania (see ALOPECIA, Vol. I, p. 339).

(b) Thinning of the nails (koilonychia) associated with gastric or *Koilonychia* duodenal haemorrhage.

I described this condition in 1921 but did not know its cause. It is now generally believed to be due to hypochromic microcytic anaemia and is curable by large doses of iron. It would appear not to be due to simple iron deficiency, since it is not seen in pernicious anaemia, in which the diminution of the iron in the blood is greater, though the colour index is high (see ANAEMIA, Vol. I, p. 408, and PEPTIC ULCER).

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ERYSIPELAS

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Reference may also be made to the following title:

ERYTHEMA

1.–DEFINITION

441.] Erysipelas is an infection of the skin involving the smaller lymphatics. The causal organism is one of the strains of the haemolytic *Streptococcus pyogenes*, and the disease is capable of spreading and resolving without loss of tissue. It is associated with well-marked constitutional disturbances, these being produced by the absorption of toxins. Although it is most commonly seen on cutaneous surfaces, it may affect mucous membranes. It is limited to the skin in a striking manner and although a form has been described (cellulo-cutaneous erysipelas) in which the cellular tissue is also affected, this should more properly be described as a cellulitis.

2.–AETIOLOGY

Entry of causal organism

The cause of the disease is the entrance of the particular micro-organism into the skin. This is effected through an abrasion or through a wound

produced accidentally or by operation. Occasionally the infection appears to gain entry through the healthy skin by means of a hair follicle. Neglected sores, such as small scalp abrasions, appear to be the commonest portal of entry. Secondary factors are always present, *Predisposing* such as a debilitated condition produced by under-nourishment, *factors* alcoholism, albuminuria, or diabetes mellitus. Underfed and neglected infants in particular are often the subject of the disease, and some individuals appear more prone than others and may have recurring attacks of the disease. In Great Britain it appears to be less prevalent than formerly and not of the same virulence; this is probably due to improved standards of living, both as regards feeding and cleanliness.

3.–MORBID ANATOMY AND BACTERIOLOGY

As already stated the organism responsible is one of the varieties of the *Causal* haemolytic *Streptococcus pyogenes*. These can be seen in groups at the *organism* advancing edges of the disease, blocking the lymphatics, while more centrally the lymphatics are seen to be choked with phagocytes actively engaged in removal of the cocci. The vessels show an inflammatory reaction, but there is not any thrombosis; oedema of the area is seen and in lax tissue may be very well marked. The lymphatic glands draining the affected part are enlarged and tender, but the inflammatory process present in the glands rarely proceeds to suppuration.

4.–CLINICAL PICTURE

The disease may affect either sex at any age but is most commonly seen in babies and elderly people. In children it is more frequent on the trunk, but in adults the face and scalp are the usual sites. The infection is *Constitutional* heralded by malaise, headache, and pyrexia, and in twenty-four hours *symptoms* there is commonly a rigor. The constitutional symptoms are out of *at onset* proportion to the clinical signs present in the early stages, and the diagnosis is not clear until the appearance of the rash.

   The rash spreads from an indolent wound, or appears on what seems *The rash* to be healthy skin. If a wound is present it may show all the signs of healing until the third or fourth day, when the rash appears and the wound breaks down. The rash has a particularly bright-red appearance, and the affected skin is slightly raised, this being most obvious at the margin, where an abrupt edge can be seen and felt. This edge is the active part and advances with considerable but varying rapidity. The previously affected part loses its brightness and shows a slight degree of pigmentation and a fine desquamation. In many cases vesicles and bullae form; these, presumably resulting from the oedema, at first contain clear serum which rapidly becomes turbid, although true suppuration does not occur. The spreading edge of the rash is usually

continuous, but in some cases a patchy condition occurs due to the rapid spread in the lymphatics, so that intervening areas of skin do not appear infected. The lymphatic glands draining the area are always enlarged. Pain is not a feature of the disease, the affected part feeling stiff and tight; but where the tissues affected are dense, such as the scalp, pain may be experienced. In the same way swelling of the part is not prominent unless the disease affects particularly lax tissues, such as the eyelids or scrotum, when considerable oedema is present.

Constitutional The accompanying constitutional symptoms are very grave, the
symptoms temperature running up to about 104° F. and showing slight variations only. The pulse in the early stages is full and usually not so rapid as would be expected with such a temperature. Delirium of a noisy type is present in the early stages. If the disease progresses the temperature remains high, the pulse becomes more rapid and poorer in quality, the delirium changes to a low muttering type, and there is well-marked prostration. In patients with a good resistance there is a moderate polymorphonuclear leucocytosis, and when this leucocytosis is absent the prognosis is gravely affected.

5.–COURSE AND PROGNOSIS

The disease lasts between one and three weeks but in some cases may continue with exacerbations for a much longer period. During this time the patient may die of exhaustion or rapidly recover under treatment. The disease alone is not fatal, but death occurs from its complications, such as visceral inflammation, especially of the kidneys and lungs, terminating in nephritis and pneumonia. It is particularly fatal in alcoholics and in poorly nourished children. The primary local condition never causes anxiety, and there is little doubt that the disease as seen in Great Britain to-day is less severe than formerly and that it is less commonly confused with cellulitis. A more chronic form is occasionally seen following an acute attack, the usual site being at the alae nasi, where a recurring fissure may cause relapses of the disease and eventually produce a persistent swelling of the face.

6.–DIAGNOSIS

Diagnosis The diagnosis is usually not difficult, as the well-marked constitutional
from symptoms, associated with the advancing bright edge of the rash and
erythematous the presence of vesicles, differentiate the disease from erythematous
eruptions eruptions. In any doubtful case the outlining of the edge with blue pencil and the examination of the edge after twelve hours usually determine the true diagnosis.

From The main difficulty usually arises in early cases of cellulitis, in which
cellulitis oedema is always present and can be demonstrated, however slight,

and the patient will usually complain of pain apart from a feeling of stiffness in the part. In some cases in which the erysipelas starts in the scalp the condition may be overlooked owing to the difficulty of examining the rash.

7.–TREATMENT

Treatment is local and general. Applications are applied to the affected *Local* area, first in an attempt to stop its spread, and secondly to give relief. *applications* The chief of these is ichthammol applied either as a 40 per cent aqueous solution, or as an ointment containing 10 per cent; whichever is used it should be renewed very often. A saturated solution of magnesium sulphate can also be applied as a lotion or cold pack. Application of ultra-violet rays to the part has very often a most beneficial effect.

The general treatment calls for active measures. The bowels must be *General* opened with a smart purge and kept open with salines. Nourishment *treatment* should be given in liquid form at short intervals; in the case of adults in whom alcohol is perhaps playing a part in the disease an adequate daily amount should be given, and this frequently averts the worst forms of delirium. Sleep is most important, and if delirium is present morphine may be injected, but better results are often attained with paraldehyde, which can be given by the rectum.

One of the most useful agents in the treatment of this disease is anti- *Antitoxin* streptococcus serum, and it seems that the scarlatinal antitoxin—i.e. streptococcus antitoxin (scarlatina)—is the best preparation to use. The fact that the antiscarlatinal serum in some cases is specific would seem to lend weight to the argument that there is a close connexion between scarlatina and erysipelas. It is often advisable, when doubt exists whether or not serum has previously been administered, to give a small dose to avoid anaphylaxis. As soon as this point has been settled, doses of 50 to 100 c.c. of serum can be given subcutaneously every day. This usually has a well-marked effect on the temperature and general constitutional symptoms. The serum treatment should be continued even after the temperature is normal, as occasionally when the treatment is discontinued there is a recrudescence of the disease.

More recently attention has been drawn to the use of compounds of *Prontosil* benzenesulphonamide in the treatment of erysipelas; and there seems little doubt that in this condition, as in streptococcal infections in general, these compounds will soon replace all other therapeutic agents. They are issued under various trade names—e.g. colsulamyde, prontosil album, prontosil soluble, proseptasine, streptocide, sulphanilamide and sulphonamide-P. They may be given by the mouth (e.g. prontosil album) or by intramuscular injection (e.g. prontosil soluble). In erysipelas oral administration is sufficient. The dose of prontosil album for adults is two tablets (15 grains) three times a day together with considerable quantities of fluid; it is important that the tablets should be chewed. For children the dose is half the adult dose and for infants a quarter,

the tablets being crushed and given in milk. The effect on the temperature is seen within 48 hours and the treatment should be continued for a few days after the disappearance of the rash. The administration of substances containing sulphur to patients receiving prontosil may result in sulphaemoglobinaemia, and is therefore contra-indicated.

Isolation and notification   Erysipelas is notifiable, and cases should be segregated. When occurring in a hospital ward the case should be isolated, and special nursing arrangements should be made, so that contact cases are prevented.

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ERYTHEMA

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Reference may also be made to the following titles:

1.–DEFINITION

442.] Erythema simply means redness of the skin, the word being derived from the Greek word for a blush, and the term may be used for any lesion of the skin showing hyperaemia with or without oedema and infiltration. Being of vascular origin the redness disappears on compression, thus differing from purpura, and, since redness is one of the cardinal features of inflammation, erythema is an early and constant sign of dermatitis or of any inflammatory reaction involving the skin.

2.–AETIOLOGY AND PATHOGENESIS

Pathogeny

According to Lewis the vasodilatation resulting from local tissue damage is due to the action of 'H'-substance, a metabolite produced on the spot, and it is thought that circulating toxins usually act upon the vessels indirectly through this substance. Further, recent work suggests that active vascular dilatation through nerve stimulation also occurs through chemical means, the ultimate stimulus presumably being 'H'-substance again. That erythema (active capillary dilatation) can be of nervous origin is certain, for example the emotional blush, and the flushed face of a patient with rosacea after a hot drink; Stricker (1876) was able to produce erythema of the skin of the limbs by stimulating the cut end of a posterior root of a spinal nerve.

The essential causes of erythema fall into three main groups: (i) noxious agents of physical, chemical, or biological nature affecting the skin from without or from within; (ii) idiopathic causes, presumably toxic, of obscure origin; and (iii) nervous causes, functional or organic.

Classification

Various authors attempt to classify the erythemas as primary or secondary, idiopathic or symptomatic, the secondary or symptomatic varieties being those of specific fevers, infection, or constitutional disturbances. Unfortunately the obscure aetiology of some varieties of erythema makes classification difficult. In spite of this it is most helpful to consider the subject on an aetiological basis, as this is essential in treatment. A further division into localized and generalized varieties can be made. As a rule localized asymmetrical erythema is due to infection or to injury from without, and the symmetrical and generalized eruptions are due to causes acting from within. Because erythema is the earliest visible sign of reaction to external irritation, its origin from this cause is generally obvious.

3.–CLINICAL PICTURE

(1)—Erythema due to External Causes
(a) Mechanical Causes

Erythema traumaticum results from pressure or friction; circumscribed red patches are commonly seen on the feet from wearing ill-fitting shoes,

beneath the pad of a truss, and at the pressure points of eye-glasses. Erythema paratrimma is the warning redness of bed-sores.

Treatment of these varieties consists in the removal of the cause, the *Treatment* use of alcohol and astringents to harden the skin, and, when necessary, the application of talc powder to diminish friction.

(b) Physical Causes

The transitory redness due to temperature changes is called erythema *Heat* caloricum and usually appears early.

Erythema ab igne is the name given to a persistent erythema of peculiar *Erythema ab* pattern which occasionally follows repeated exposures to radiant heat *igne* (infra-red rays) and less often the local application of heat such as by means of a hot-water bottle. The erythema appears as a coarse network enclosing pale areas corresponding to those directly supplied by an
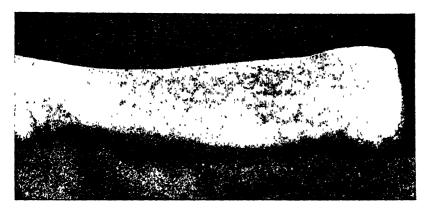
FIG. 15.—Erythema ab igne. (Dr. O'Donovan's case)

arterial tree (see Fig. 15), and it is thought that the diminished tone of the capillaries remote from the arterial stream accounts for the erythema and its pattern, as these vessels are more susceptible to damage and react by dilatation, remaining in a state of chronic congestion. Later a brownish colour takes the place of the red, and the condition may then be called ephelis ab igne. Extravasation of blood pigment is the obvious explanation of the clinical appearances, but inflammatory changes have been reported and the presence of brown pigment noted in the cells of the basal layer of the epidermis.

Erythema ab igne is most often seen on the front of the legs as a result of toasting them before a fire. The pigmentation fades slowly and does not require any treatment.

Degrees of cold which freeze the skin are invariably followed by ery- *Cold* thema and inflammatory changes which may culminate in a bullous dermatitis, ulceration, or gangrene. Such reactions are seen after frost-bite and the application of solid carbon dioxide or liquid air. Lesser degrees of cold give rise to various erythematous conditions, which may not be the effect of cold alone but depend upon local alterations of

vessel tone or tissue vitality. Tuberculous subjects are particularly prone to abnormal responses to cold. In other cases chronic infections, toxaemias, endocrine disorders, and diseases of the nervous system are occasional disposing factors.

The commonest reaction to cold is an erythema which quickly deepens to a purplish or blue colour and in children usually appears on the extremities. As a result of venous stasis the eruption often presents a

Livedo coarse reticular pattern and is known as livedo reticularis or livedo annularis; and this, although quite common in otherwise healthy children, should if persistent be regarded as an indication for excluding the predisposing factors mentioned above. General tonics, such as iron, calcium, phosphorus, strychnine, vitamin D, and ultra-violet irradiation are indicated.

Perniosis Perniosis is a convenient collective term for a group of conditions in which apparently the prolonged effect of cold is merely the exciting cause. Under this heading are included acrocyanosis, erythema pernio, and erythrocyanosis.

Acrocyanosis In its fully developed form acrocyanosis is a true cyanosis of the extremities associated with a feeling of cold and a slow return of the colour to the skin after compression. Erythema is the earliest sign and the amount of blueness varies considerably. The condition is mentioned here because persons with red or blue cold hands are more prone than others to develop chilblains, and the underlying factors in each of these conditions probably are the same.

Erythema pernio Erythema pernio or chilblain occurs as rounded circumscribed slightly raised red plaques, usually hot and indurated, on the extremities of predisposed people. Vesication or blister formation may develop with ulceration in severe cases. The incidence is highest in cold damp weather, but very susceptible persons seem to get attacks with slight variations in barometric pressure too. The fingers and toes are most often affected, then the ears, where ulceration is frequent; sometimes the tip of the nose is involved, and more rarely lesions appear on the arms, legs, and buttocks. Itching is early and constant, and exacerbations occur when the skin gets hot, especially if woollen socks or stockings are worn. Pain and burning sensations are present in varying degree and these symptoms together with the well-known local appearances make the diagnosis easy. For treatment see CHILBLAINS, Vol. III, p. 121.

Erythrocyanosis crurum puellarum Erythrocyanosis crurum puellarum often causes difficulty in diagnosis (see CHILBLAINS, Vol. III, p. 121, and ERYTHROCYANOSIS, p. 183).

Erythema due to radiant energy Among the physical agents producing erythema, the various forms of radiant energy are of particular interest (see Vol. III, p. 610).

Beginning with the waves of moderate length, familiar as so-called short-wave radio, is short-wave diathermy which has a direct heating effect on the skin and, like the infra-red rays (radiant heat), rapidly produces an erythema. On the other hand, erythema resulting from exposure to ultra-violet rays may not appear until six hours or more afterwards, and its sudden onset after this latent period may be perplexing.

Erythema solare or sunburn is really due to the ultra-violet rays, but *Erythema* the presence of radiant heat augments their action. Pigmentation affords *solare* protection against these rays, with the result that blonde types who do not become pigmented suffer more than brunettes. The erythema is most marked on those parts directly exposed to the sun, but anomalous cases occur in alpine districts where the ultra-violet rays, being reflected from snow and ice, produce sunburn on the lower parts of the face.

Preventive treatment consists in avoiding direct exposure to sunlight and protecting the skin by applying emollient preparations which are opaque to the ultra-violet rays or which by fluorescent properties increase the wave-lengths. Calamine lotion or liniment is useful, and nut-oil, yellow soft paraffin, and the soluble salts of quinine are used for their fluorescent effects. Tannic acid 10 per cent and castor oil 2 per cent in industrial methylated spirit is an excellent prophylactic paint.

After exposure to X-rays or radium, erythema may not appear for two *X-rays and* to three weeks, but if so delayed it is of mild degree. The earlier after *radium* irradiation that erythema appears the graver its significance, and it may progress rapidly to painful and intractable ulceration or slowly to severe atrophy of the skin. In this form of erythema it is essential to avoid any further irritation of the skin and only the blandest applications should be used. As a rule lotions are tolerated better than ointments.

(c) Chemical Causes

These may be classified as: (i) caustics and corrosives, such as the alkalis and strong acids; (ii) rubefacients, such as cantharides, capsicum, croton oil, turpentine, and mustard; and (iii) substances to which some individuals have an idiosyncrasy, the common ones being iodine, mercurial salts, picric acid, salicylic acid, and chrysarobin; but no doubt almost every local application has produced erythema and dermatitis in some subjects (see Vol. III, p. 613, and Vol. IV, p. 266).

(d) Animals and Plants producing Erythema

It is well known that contact with hairy caterpillars and jelly-fish may *Animals* produce a brisk local erythema; these lesions itch and may proceed to oedematous inflammatory reactions with the later appearance of erythematous patches on other parts of the body. The handling of some fish produces similar effects, which are attributed to puncture from prickly spines. Focal erythematous lesions are the earliest results of insect bites and when the exposed parts of the limbs are attacked symmetrical eruptions result which may simulate toxic rashes. (See also BITES AND STINGS, Vol. II, p. 343.)

The common stinging nettle (*Urtica dioica*) is the most obvious example *Plants* of a plant producing erythema, but more interesting are the innumerable other plants which produce dermatitis venenata in sensitive subjects, the first manifestation being an erythema. It is most important to consider the possibility that an acute erythema of the face, hands, or

forearms may be of plant origin; confirmation can usually be obtained by patch testing, which merely entails strapping a part of the suspected plant to the subject's skin for twenty-four to forty-eight hours, when an erythematous reaction denotes a positive result. (See Vol. III, p. 613, and Vol. IV, p. 449.)

(e) *Erythema associated with Systemic Infections*

Pathogenic organisms
Fungi, bacteria, and viruses often produce erythematous lesions at the portal of entry; but the skin can be invaded just as readily from the lymphatics or blood-stream, and in many cases it is impossible to decide whether infection occurred from without or from within. Erythema is quickly followed by the classical signs of inflammation, and it is unnecessary to discuss every possible localized infection. The most striking erythematous one is erysipelas, and the diagnosis of this from an acute

Erysipelas
oedematous dermatitis may be difficult. Constitutional effects are more marked in erysipelas, the affected area is more indurated and usually has a well-defined edge, and vesicles and bullae may be present. If a dermatitis venenata becomes vesicular, the vesicles usually occur in groups and quickly rupture and form weeping points or small plasma crusts; the skin is neither so hot nor so tense as in erysipelas (see p. 155).

Erythema as symptom of other infections
Erythema, local or general, occurs as a symptom in a number of infections. In many of these, the infecting agent not having been demonstrated in the skin lesions, it is probable that the erythema is toxic in origin. This group therefore makes a useful introduction to the study of the erythemas of obscure origin and many analogies will be observed. As the cause, whether toxic or infective, is internal, the resulting lesions are likely to be symmetrical, but areas of skin exposed to cold, heat, light, or any form of irritation may be more reactive and produce anomalous patchy or asymmetrical eruptions. Similarly, since the erythematous response depends upon intact vascular and nervous mechanisms, lesions of vessels or nerves may account for a perplexing picture. These observations apply to all erythematous eruptions however produced.

Localized
Localized erythema or small erythematous macules occur in the following systemic infections with viruses, bacteria, or protozoa: cerebrospinal fever, enteric, chicken-pox, smallpox, dengue, leprosy, malaria, syphilis, and tuberculosis among many others.

Generalized
Generalized erythema or erythema in sheets occurs in scarlet fever, measles, German measles, and more rarely in acute rheumatism. Many of the above conditions may be recognized by characteristic lesions which develop quickly from the initial erythematous macule, but scarlet fever is closely imitated by a number of widely spread erythemas of drug or presumably of toxic origin. Generalized erythema of toxic origin will be discussed later, but one type of localized erythema usually ascribed to tuberculous infection, namely, erythema induratum, will be considered here.

(f) Erythema Induratum
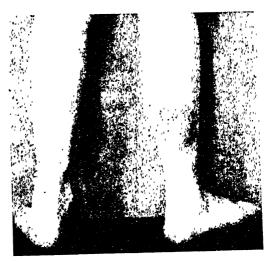
(Synonym.—Bazin's disease)

Erythema induratum is a chronic condition almost exclusively affect- *Definition* ing the legs of young women and is characterized by firm, nodular, and symmetrical subcutaneous infiltrations which tend to break down into indolent ulcers.

The condition usually begins in adolescence and is most apt to affect *Aetiology* girls and young women who are susceptible to chilblains, are poorly nourished, and have to stand at their work. It would appear that the perniotic condition permits the development of a local tuberculous

granuloma. The presence of tubercle bacilli in the lesions is demonstrated with difficulty, but a number of authorities (Eyre; Fox; Gilchrist; Ravaut) have successfully inoculated guinea-pigs, although acid-fast bacilli have not been seen in sections.

Morbid anatomy

The histological appearances usually suggest tuberculosis, and collections of epithelioid cells and occasional giant cells form characteristic tubercles. Focal necrosis occurs and is probably secondary to vascular changes, the vessels being thickened with well-

FIG. 16.—Erythema induratum (Bazin). The lesion on the right leg is more advanced than that on the left and its square shape is characteristic of a reaction to a local application; the primary lesions are seen in the posterior edge. (Dr. Sequeira's case)

marked perivascular infiltration. Elastic and collagen fibres are destroyed, and some of the adipose tissue is replaced by the infiltrate.

The subjects usually have rough dry skins with prominent follicles. *Clinical* Thickened subcutaneous tissues make unshapely ankles. The sites of *picture* election are the posterior and lateral aspects of the lower half of both legs (see Fig. 16); more rarely the fronts of the legs are affected and even the thighs and arms. A palpable induration is the earliest sign, and soon an erythema appears over it and darkens to a purple or bluish tint. Usually separate nodules develop and attain a size of 1 to 3 cm.; the colour darkens as the process reaches the surface, and then the bluish centre breaks down discharging clear or sero-sanious fatty fluid to form an indolent ulcer. The ulcer has an irregular margin, a sharply cut slightly undermined edge, and a flat greyish or red base with a surrounding zone of purplish discoloration and infiltration. Healing is slow

during winter months, and finally a sunken brownish scar remains, which in course of time becomes pale and may have a pigmented zone around it. Pain is rarely severe.

Course and prognosis
The course and prognosis vary greatly in different persons, and the determining factors appear to be the degree of perniosis present and the extent and activity of tuberculous foci. Mild cases clear up each summer and relapse each winter, and with treatment these respond well. Severe cases may have ulcers of five to ten years' standing which resist all routine measures of treatment, and many intermediate types occur.

Diagnosis from erythema nodosum
Erythema nodosum is much more acute; the lesions appear over the anterior tibial muscles, are tender and painful, and do not ulcerate; the patient suffers from malaise, fever, and often joint pains.

From tertiary syphilis
In tertiary syphilis gummata usually occur later in life, are asymmetrical, and usually affect the fronts of the legs, but the clinical appearances may be very suggestive of Bazin's disease, and the syphilitic origin is only revealed by blood tests and (or) the response to specific therapy. The purple cyanotic tints of Bazin's disease are absent in gummata.

From mycotic granulomas
Mycotic granulomas are generally asymmetrical; the diagnosis depends upon finding the organism. (See also ACTINOMYCOSIS, Vol. I, p. 173, BLASTOMYCOSIS, Vol. II, p. 403, and FUNGOUS DISEASES, p. 448.)

From iodide granuloma
Iodide granuloma is commoner in elderly subjects, and inquiry should be made whether any drug is being taken (see DRUG ERUPTIONS, Vol. IV, p. 268).

Treatment
Preventive measures consist of exercises and the wearing of thick stockings to keep the legs warm, a full diet adequate in iron, calcium, phosphorus, and vitamins A and D, and the avoidance of long periods of standing at work.

Some good results have followed specific treatment with tuberculin, using minute doses cautiously increased.

Lumbar ganglion-ectomy
Dickson Wright advocated lumbar ganglionectomy in severe cases and claimed that the success of this surgical procedure indicated that Bazin's disease had a vasomotor and not a tuberculous aetiology. The histopathology and the therapeutic response to tuberculin alone in some cases are opposed to this view, but dermatologists do not deny the importance of the vasomotor mechanism, which produces a perniotic background for the tuberculous process. Moreover, much of the treatment advocated is also that recommended for chilblains.

Physio-therapy
Physiotherapy is often helpful, especially general ultra-violet light and local infra-red irradiation and massage. The last-mentioned can be made automatic by the application of firm elastic adhesive bandages, which also assist by keeping the skin warm. Small doses of X-rays, $\frac{1}{3}$ pastille B. dose (100 to 120 r. at 90 k.v.), may also be given and repeated three times at intervals of two to three weeks.

Drug
The ulcers often respond to red mercuric oxide ointment. If this is too strong, boric acid ointment with eucalyptus oil 10 minims to the ounce may be substituted or ichthammol 20 grains in one ounce of zinc paste B.P. However, when the ulcers tolerate occlusion with adhesive band-

ages they are best left covered for a week or more at a time. Occasionally a few weekly injections of neoarsphenamine, 0·3 to 0·6 gram, cause rapid healing, although no evidence of syphilis exists. The response should not be taken as an indication of a luetic infection.

Small doses of thyroid may be tried, too, with doses of syrup of ferrous *Thyroid* iodide thrice daily. If general light therapy is being given it is well to ensure an adequacy of iron, phosphorus, and calcium by prescribing compound syrup of glycerophosphates B.P.C. or compound syrup of hypophosphites B.P.C.

Severe ulcerative cases respond best to prolonged rest in bed, and *Rest* healing can usually be secured by this means.

(2)—Erythema due to Internal Causes
(a) Drugs

In the discussion of erythema due to chemical irritation drugs with *Drug* rubefacient properties were included, but no mention was made of ery- *eruptions* thematous eruptions due to drugs ingested. A list of the common drugs causing erythema is given in Vol. IV, p. 266, and the view is expressed that many if not all of the eruptions are not due to the drug itself but probably to some secondary toxic cellular product, this fact explaining why many drug eruptions have exact counterparts in certain toxic rashes. For instance, if a patient begins an arsenical dermatitis, the first *Arsenical* lesions appear on the flexor aspects of the forearms as erythematous *dermatitis* *mimicking* macules which irritate. The erythematous rash spreads symmetrically *other* on the arms, then affects the face and neck, and finally may involve the *eruptions* trunk and lower limbs. In severe cases the erythema becomes wide-spread and tends to desquamate early, thus helping to distinguish the condition from scarlet fever (see secondary erythrodermia, p. 174).

Another less serious eruption sometimes arises on the ninth or tenth *'Erythema of* day after the first injection of arsenic in the treatment of syphilis. This *the ninth day'* 'erythema of the ninth day' appears as a rapidly spreading scarlatiniform eruption with little irritation. The rash lasts a few days only, without desquamation, and does not recur with further arsenical treatment (Gordon).

Erythematous toxic eruptions affect mainly the trunk, upper arms, and *Erythematous* thighs, and present various lesions from the large sheets of scarlatiniform *toxic erup-* *tions in* type through smaller macular lesions of different sizes and shapes to *general* minute pin-head spots. Sometimes the eruptions are slightly oedematous and might reasonably be regarded as urticarial, but this distinction between toxic rashes is of no practical importance. Toxic rashes usually erupt quickly and begin to fade in a few days, leaving brownish macular staining and as a rule slight desquamation. Some irritation is usually present and may precede the eruption and, since the skin reaction is but a manifestation of a general intoxication, there may be malaise, vomiting, diarrhoea, slight fever, and joint pains.

(b) Food, and Intestinal Toxaemia

Apart from drug eruptions and the rashes associated with general infection already mentioned the following are common causes of toxic *Erythematous* rashes: (i) Certain foods, such as shell-fish, mushrooms, tinned meat or *toxic erup-* fish, and acid fruits, e.g. strawberries and plums; small seasonal epi- *tions due to* demics of toxic eruptions occur when certain foods are plentiful and *food* diagnosis becomes increasingly easy. (ii) Intestinal toxaemia is strongly *Alimentary* suggested when a rash follows vomiting, diarrhoea, or both, and the *toxaemia* well-known enema rash is ascribed to increased absorption of toxic faecal products. So in the absence of other causal factors it must often be assumed that the toxin is an alimentary one, and successful treatment with aperients, antiseptics, and adsorbents (charcoal and kaolin) seems to justify this assumption. Hydatid or tapeworm infection may also account for a toxic erythema.

Other toxic Certain toxic erythemas exhibit peculiar features, and upon these *erythemas* special clinical varieties have been established. The two best known are erythema multiforme and erythema nodosum.

(c) Erythema Multiforme

(Synonym. Erythema exudativum)

This is a toxic eruption characterized by erythematous patches of various shapes, patterns, and sizes accompanied by serous exudate producing elevated lesions and frequently vesicles and bullae.

Aetiology It is commonest in children and adolescents and shows a seasonal incidence in spring and autumn. The causes are those already enumerated for toxic eruptions, but foods and drugs are rare causes, whereas bacteria and their toxins and antitoxins are common. Some regard it as evidence of a rheumatic infection, because it is at times associated with acute rheumatism and at other times with arthritis, endocarditis, chorea, and tonsillitis; but its aetiological basis is obviously broader than that. Not uncommonly the eruption appears without any discoverable cause, as the only symptom in a healthy subject.

Morbid The essential changes may be explained by the action of circulating *anatomy* toxins upon the small vessels or upon the nerves controlling them, resulting in dilatation and exudation of plasma, the latter causing oedema of the prickle-cell layer and forming vesicles or blebs at various levels in the epidermis. A cellular infiltration is most prominent about the dilated vessels and may reach the deepest layers of the corium and also invade the epidermis, making the vesicles and blebs cloudy and purulent. Erythrocytes may escape from the vessels and colour the lesions.

Clinical Sometimes the eruption appears without any general disturbance, but *features:* usually the onset is marked by malaise and a slight degree of fever. Pain *general* and swelling of the larger joints may occur, and also sore throat, vomiting, and diarrhoea; but the more severe constitutional symptoms often denote the presence of some definite infective disease.

The eruption usually appears suddenly and is symmetrical (see Fig. 17). *Local* It commonly affects the dorsal surfaces of the hands and feet, the extensor surfaces of the arms and legs, the knuckles, wrists, and knees, and at times the face and neck. Other parts may be involved, and not uncommonly the mucous membranes of the lips, tongue, cheeks, and pharynx show red macules, papules, vesicles, and superficial erosions.

The simplest lesions are dark-red macules, round or oval and sharply *Types of* defined. Exudation produces papules or raised plaques, and vesicles or *lesion* bullae may arise later. Although all these forms are often found together, usually one type of lesion predominates; this accounts for a number of names which are merely descriptive.

Erythema papulatum refers to one form presenting dome-shaped papules about 0·5 cm. in diameter. *Erythema papulatum* Larger nodular forms occur and may be described as erythema tuberculatum or erythema tuberculosum — confusing terms best avoided.

Erythema circinatum consists of ringed lesions with a pale centre and a red margin which may be narrow, vivid, and raised, presenting a striking appearance. The coalescence of two or more rings produces gyrate patterns termed erythema figuratum. *Erythema circinatum*

FIG. 17.—Erythema multiforme. (Dr. Sequeira's case)

Erythema iris (see Fig. 18) is *Erythema* characterized by concentric rings *iris* resembling a target or the iris and pupil of the eye. The colour of the centre varies from rose-pink to purple, and the centre may be vesicular or haemorrhagic. Around this occur two or more zones alternately dark or pale, the usual size being between one-half to three centimetres. This form is perhaps the best known, because recurrences are quite common and may be frequent.

Erythema vesiculosum and erythema bullosum are self-descriptive. *E. vesiculosum and e. bullosum*

Erythema purpuricum is a more severe toxaemia in which haemorrhages occur into the erythematous spots or central blebs; in a patient *Erythema purpuricum* under J. H. Sequeira haematuria occurred at the same time.

The disease runs an acute course of one to four weeks and leaves no *Course and prognosis* trace on the skin, although some desquamation or pigmentation may persist temporarily. Recurrences may occur, particularly in the iris type.

Diagnosis is not difficult as a rule, because the slight prodromal *Diagnosis* symptoms and the sudden appearance of the circumscribed red patches on the extremities, with little irritation, are very suggestive. Soon the

variations in the patterns and colour tones of the lesions make the multiform character obvious.

From lupus erythematosus   Lupus erythematosus may be suggested by the red macular type, but the former eruption most commonly occurs on the central part of the face and the fingers; the lesions are dull, scaly, purplish, uniform in type, and very persistent.

From urticaria   Urticaria resembles the papular and oedematous types, which histologically are urticarial reactions, but clinical urticaria is common
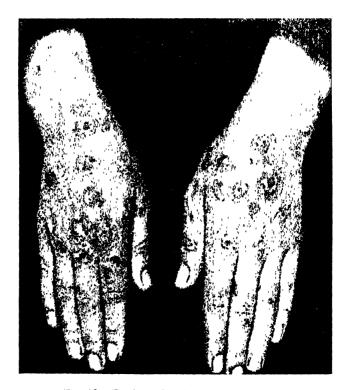
FIG. 18.—Erythema iris. (Dr. Whitfield's case)

enough to be well known; its lesions are uniform, transitory, less erythematous, and more irritating.

From tinea circinata   Tinea circinata is differentiated from the circinate and annular erythemas by its scaly uneven edge, which is made up of vesicles and pustules. In doubtful cases microscopical examination of scrapings of the edge for the presence of fungus should be made.

From dermatitis herpetiformis and pemphigus   Dermatitis herpetiformis and pemphigus may be closely imitated by the bullous varieties of erythema multiforme, but these are generally very chronic, and the diagnosis becomes clear with the passage of time.

Treatment   The first essential in treatment is to consider every possible cause and by careful inquiry and examination to eliminate a food, drug, or inflammatory origin. When the condition is associated with bacterial or protozoal infections, general treatment is merely for those, e.g. quinine for malaria, and in rheumatic conditions salicin and salicylates. In cases

of obscure aetiology or if gastro-intestinal symptoms are present, alkalis, aperients, intestinal antiseptics and adsorbents should be tried, for example: white mixture, mercury with chalk 1 grain three times a day, or medicinal kaolin or charcoal. A diet very low in protein should be taken. Warm alkaline baths are helpful.

Local treatment consists in the application of cooling and sedative lotions such as calamine with strong solution of lead subacetate 5 minims to each fluid ounce, or solution of coal tar 10 minims with glycerin 30 minims to 1 fluid ounce of dilute solution of lead subacetate.

(d) Conditions allied to Erythema Multiforme

Closely resembling the circinate forms of erythema multiforme are a number of chronic eruptions, and amongst them it would appear that identical conditions have received different names from different observers.

Erythema annulare centrifugum

Erythema annulare centrifugum of Darier is usually seen as large rings with smooth, pink, cord-like edges which slowly move in a centrifugal manner and occasionally the lesions can be observed evolving from a papule which resolves in the centre and spreads peripherally. The eruption may last six months or more.

Erythema chronicum migrans

Erythema chronicum migrans is a similar ringed eruption with a larger pattern; but as some of these cases have been sequelae to insect bites they may be infections of the skin.

FIG. 19.—Erythema elevatum diutinum. (Dr. O'Donovan's case)

Erythema figuratum perstans and erythema gyratum perstans refer to very similar conditions but usually the edges of the lesions are broader and flatter and the lesions themselves more numerous. *Erythema figuratum perstans*

Granuloma annulare is probably allied to these chronic ringed eruptions, although its edge is more papular like the lesions of erythema elevatum diutinum of Radcliffe Crocker and Campbell Williams (see Fig. 19). *Granuloma annulare* *Erythema elevatum diutinum*

It is generally thought that all these eruptions are toxic in origin with the same aetiological factors as erythema multiforme but they give much less satisfactory responses to treatment. Whether these conditions are clinical entities is still a matter of controversy in dermatological circles.

(e) Erythema nodosum

This is a toxic eruption characterized by the formation of symmetrical nodular erythematous swellings on the extensor aspects of the limbs.

Aetiology

It is thought by many to be a variety of erythema multiforme, though anomalous because the lesions are of a solitary and constant type. There are many recent references in the literature to its association with tuberculosis, and some authorities regard it as essentially a tuberculous manifestation. Goldsmith from a review of the evidence concluded that, although a tuberculous infection predisposed to erythema nodosum, the eruption was not essentially a tuberculous manifestation. Similar eruptions are seen in acute fevers and especially with streptococcal infections (Forman) and have followed the ingestion of drugs, notably iodides, bromides, and antipyrin. Moreover, Sequeira reported that 20 per cent of his cases of erythema nodosum were associated with rheumatic fever, so that the only common factor in these associations is a toxic one, and a specific infective cause is improbable.

Like erythema multiforme the disease is more common in the spring and autumn; females between ten and thirty are most commonly affected.

Morbid anatomy

The morbid anatomy is essentially similar to that of erythema multiforme, but the whole thickness of the skin and subcutaneous tissues is involved. Cellular infiltration and exudation are more prominent, and red blood cells or actual haemorrhages are also often present, the latter accounting for the staining apt to mark the site of resolved lesions.

Clinical picture
General symptoms

The onset of the eruption is preceded by malaise, gastro-intestinal disturbances, fever, and joint pains of the rheumatic type. These symptoms may be slight or more rarely severe with hyperpyrexia, rigors, and delirium. The eruption is symmetrical and appears abruptly, most often about the middle of the legs, over the anterior tibial muscles, occasionally below the elbows, and rarely on the thighs, upper arms, and face.

Skin lesions

The skin lesions are acute inflammations, being red, swollen, hot, painful, and very tender to touch; they are oval or round, slightly dome-shaped with a tense shiny surface, and the induration indicates the depth of infiltration. Evolution is rapid, and in twelve to twenty-four hours the colour may be fading and the tenseness gone, but the node can be seen and felt for a week or more, and some staining and slight desquamation mark the site for several weeks. New crops may appear and prolong the disease. Ulceration never occurs, and eventually nothing remains to bear witness to the attack. Recurrences are rare.

Diagnosis

Diagnosis is easy as a rule. The symmetry rules out acute local infection, such as erysipelas, cellulitis, or abscess, and at the same time the acute inflammation distinguishes it from the granulomas. Erythema induratum (see p. 165) is chronic, relatively painless, and often ulcerated.

Treatment

Complete rest with the diet and nursing of a fever are advisable. Quinine, aspirin, salicin, and alkalis may be useful. Local measures are limited to the application of such cooling lotions as lead lotion or a 2 per cent solution of aluminium acetate.

(*f*) *Erythema associated with Pellagra and Pink Disease*

Some localized erythemas presumably of toxic origin are fairly characteristic of definite diseases, two well-known examples being pellagra

and pink disease. In pellagra the eruption appears on parts exposed to *Pellagra* light, the hands, face, and neck being most affected. The erythematous areas are well defined, usually burn or itch, and later show desquamation and pigmentation. The sharp margin is a characteristic feature. In pink *Pink disease* disease the same parts are affected, the hands being bright-red and swollen. Attention has been drawn to the importance of nervous and vascular influences in the production of the erythematous reaction; and the fact that these operate most strongly at the extremities makes it difficult to elucidate the mechanism responsible for the erythematous condition of the hands and feet.

Erythromelalgia probably results from such nervous and vascular influences alone and has some analogy to Raynaud's disease, which also has early erythematous phases.

In the discussion of the types of toxic erythemas mention was made of patchy scarlatiniform eruptions, but one form is regarded as a clinical entity and bridges the gap to the so-called erythrodermias.

(g) Erythema Scarlatiniforme

As the name implies, this eruption closely resembles that of scarlet fever. The causes are those mentioned for the toxic eruptions (see p. 167), *Aetiology* interesting examples being quinine by the mouth, mercury by inunction, iodoform by local application, various infections, and even enemas.

Constitutional effects depend upon the essential cause; when this is an *Clinical* infection, malaise and moderate fever usually precede the eruption by *picture* a day or two, but in other cases the eruption is the first sign. The rash is often indistinguishable from that of scarlet fever but less extensive, and desquamation appears early, by the second day in some instances. Subacute and recurrent forms occur, and sometimes the scaling is gross, casts of the hands and feet being shed and rarely the nails and hair.

The course is short, the rash disappearing in twenty-four hours or *Course* lasting up to a week and sometimes continuing as an exfoliative dermatitis. Recurrent attacks tend to be less severe.

The usual and sole difficulty in diagnosis is to distinguish the condition *Diagnosis* from scarlet fever, the greater constitutional effects in the latter disease *from scarlet fever* being deciding features. The onset with headache and vomiting, the swollen inflamed fauces, the adenopathy, and the characteristic furred tongue with its various phases all suggest, and a subsequent desquamation confirms, scarlet fever. A recurrence is rare in the exanthem.

Treatment depends upon the cause and is the same as that laid down *Treatment* for the other types of toxic eruptions.

(h) Erythrodermia

This name is usually reserved for the extensive or general erythemas associated with various degrees of scaling and cellular infiltration of the dermis. Quite often the cause of the condition and the clinical and histological pictures of the reaction are identical with or very similar to those of the toxic erythemas. Primary and secondary forms are described, and the latter will be discussed first.

Not infrequently the erythematous eruptions due to arsenic pass from the localized forms mentioned into a general erythema with exfoliation; the skin is infiltrated and thickened, and the condition is then a true erythrodermia. Similar conditions with less scaling also occur after toxic reactions to gold, mercury, bismuth, and antimony given internally, and to certain drugs, such as chrysarobin and oil of cade, applied to the skin, although in the latter instances the underlying condition, usually psoriasis, is probably the determining factor. Even without treatment by irritants psoriasis is occasionally followed by a general exfoliative dermatitis (or erythrodermia) which may persist for years, and more rarely the same eruption is a sequel to seborrhoeic dermatitis, pityriasis rubra pilaris, or lichen planus. In such cases evidence of the primary disease often exists, the erythrodermia runs a benign course, and with its disappearance the original disease may reassume its ordinary character. On the other hand, such secondary erythrodermias occasionally run an acute course; rapid wasting indicates a grave toxaemia with a fatal issue, thus showing no essential difference from a primary erythrodermia.

Treatment The treatment apart from that of the primary skin disease is on the same lines as that to be discussed for the next group.

Erythrodermia also occurs as a rare premycotic phase of mycosis fungoides, but in this disease the unusual feature of intense itching which probably preceded the eruption suggests the diagnosis. The lymphatic glands may be enlarged, but the blood count distinguishes the condition from leukaemia, which very rarely simulates it, and the late appearance of tumours is quite characteristic. Sequeira and Panton described a *Lympho-
blastic ery-
throdermia* series of cases of lymphoblastic erythrodermia, of which the striking feature was a relative and absolute increase of the lymphocytes, especially the small lymphocytes (which were as high as 80 per cent of total counts of 8,000 to 60,000). The skin in their cases was described as of a dull rose-red brick colour with scaling. Pruritus was a prominent feature. Glandular enlargement was present in all but never to the extent seen in chronic lymphoid leukaemia. The disease ran a chronic course over some years and was unaffected by treatment. These cases of lymphoblastic erythrodermia are still by some regarded as manifestations of chronic leukaemia, and the relatively low white count is ascribed to an aleukaemic phase. As a matter of fact erythrodermia is a very rare complication of leukaemia, and when it does occur it is usually scaly and the skin is appreciably infiltrated. Skin infiltration with nodule and tumour formation may occur in myeloid leukaemia, but it does so without erythrodermia and has a characteristic blood picture associated with it. In Sequeira's cases lymphocytic infiltration of the skin only occurred in the last stages, which is a further distinction. Diagnosis is difficult in this group, and in all cases examination should include the spleen and lymphatic glands, repeated differential blood counts, and when possible biopsy of the skin and glands.

A congenital form of erythrodermic xerodermia has been described

in which the ordinary type of xerodermia is coloured by a general *Primary* erythema. In infants this type must be distinguished from the acquired *erythro-* exfoliative dermatitis of Ritter (see Vol. III, p. 623). *dermias*

The acquired erythrodermias may either be acute or chronic, the former being represented by the recurrent variety of scarlatiniform erythema (see p. 173).

The chronic varieties are two types of exfoliative dermatitis which have sufficiently constant clinical features to be regarded as clinical entities, although it is doubtful if their aetiology is constant. Thus cases arise as described under secondary erythrodermias, and the skin condition progresses and becomes fixed in a chronic state quite indistinguishable from that about to be described. The probable explanation is that the skin is reacting to some toxin.

(i) *Exfoliative Dermatitis*

The exfoliative dermatitis of Erasmus Wilson is a subacute type in *Exfoliative* which an erythema tends to become general and the skin sheds large *dermatitis of* sheets of thick scales. The only reason for regarding this condition as *Wilson* primary is that it arises without obvious cause, although a number of cases have followed fright or exposure to cold. No clinical difference marks the secondary cases which follow, for example, intravenous arsenic or inunction of chrysarobin, and the division into primary and secondary types is therefore academic rather than practical.

Pityriasis rubra of Hebra and Jadassohn is a more chronic form of *Pityriasis* exfoliative dermatitis, but the distinction between it and the condition *rubra* associated with the name of Erasmus Wilson is often difficult. (See also DERMATITIS, EXFOLIATIVE, Vol. III, p. 619.)

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ERYTHRAEMIA

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Reference may also be made to the following titles:

ANAEMIA   BLOOD EXAMINATION   LEUKAEMIA

1. DEFINITION

(*Synonyms.*— Polycythaemia vera; splenomegalic polycythaemia; Vaquez' disease; Osler's disease)

443.] Erythraemia is a rare disease characterized by polycythaemia, increased viscosity and volume of the blood, cyanosis, and spleno-megaly.

2.–AETIOLOGY

Maximum normal blood count

Polycythaemia may be defined as an excess of erythrocytes in the blood. The upper limits of a normal blood count may be considered to be approximately six million cells and 120 per cent haemoglobin. Figures above this limit are found in various conditions, of which erythraemia is one of the most uncommon; hence it is essential to consider the general problem of polycythaemia. An increase of red cells may be an

Causes of increase of red count

absolute increase or an increase per unit volume. An example of the

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latter is the polycythaemia secondary to concentration of the blood con- *Relative* sequent on severe sweating, vomiting, or diarrhoea. Another example *and absolute increase* is the high red cell count found in persons with chilblains and Raynaud's disease when blood is taken from the area of local congestion. Capillary stasis causes concentration of the blood in the affected areas. An absolute increase of red cells results from one of two causes: (i) a primary disease of the erythroblastic tissues, analogous to the hyperplasia of the leucoblastic tissues in leukaemia—hence the name erythraemia; and (ii) a compensatory hyperplasia of the erythron secondary to factors which lead to incomplete oxygenation of the blood. The term erythrocytosis should be confined to this latter type of polycythaemia. The conditions disposing to erythrocytosis are chronic heart and lung disease, either congenital or acquired, residence at high altitudes, and the toxic effects of various poisons, e.g. carbon monoxide, phosphorus, and aniline dyes. A rare syndrome in which erythrocytosis *Ayerza's* is a feature was first described by and is called after Ayerza of Buenos *disease* Aires. The syndrome should include only those cases in which polycythaemia can be shown to be dependent upon pulmonary arteriosclerosis. It is probable that the arteriosclerosis may be due to more than one cause, but it is generally agreed that the most important factor is syphilis. A diagnosis of erythraemia should never be made till the commoner conditions which cause erythrocytosis have been first excluded.

Erythraemia was first described by Vaquez in 1892, but it was the publications of Osler (1903–1904) which made the condition widely known.

Males are said to be affected more often than females; the age of onset *Age and sex* is in middle life, most cases occurring between the ages of thirty-five *incidence* and sixty-five. A familial trait is occasionally found; the disease is stated to affect chiefly people of spare build with thin narrow faces and fair complexion. The cause of the primary hyperplasia of the erythroblastic tissues is unknown.

3.–MORBID ANATOMY AND BLOOD PICTURE

The erythroblastic hyperplasia is shown by the deep-red appearance and great extension of the red marrow in the long bones. The leucoblastic tissue is likewise increased. The lymphatic glands are not enlarged, but the spleen is usually increased in size, sometimes to a marked degree, as the result of hyperplasia and congestion of the pulp. Infarcts are common. Moderate enlargement of the liver due to engorgement with blood is found; arteriosclerotic changes in blood-vessels are often present, and in such cases cardiac hypertrophy, with or without degenerative changes in the heart-muscle, occurs.

The red cell count is usually from 7 to 12 million cells, the highest *Blood* authentic count being 13,600,000. The haemoglobin varies from 120 to *changes: red cells* 160 per cent, and the colour index ranges from 0·7 to 0·9. Examination

of the stained film shows that the erythrocytes are either normal in size, or, more often, slightly smaller than normal; immature cells (normoblasts and reticulocytes) are present in excess of the normal, reflecting the hyperplastic reaction of the bone marrow.

Leucocytes　　The leucocyte count is increased, varying from 10,000 to 30,000 cells per cubic millimetre, with 75 to 85 per cent of polymorphonuclear leucocytes. In some cases the presence of immature cells (myelocytes) in considerable numbers makes the differential diagnosis from leukaemia difficult. There would appear to be some relationship between the diseases, because Naegeli stated that all cases of leukaemia started with a polycythaemia. In addition, some cases of polycythaemia have terminated with a typical clinical, haematological, and pathological picture of leukaemia. The platelets are normal or increased in number.

Other blood tests　　The sedimentation rate of the erythrocytes is slow; the tests for fragility, bleeding time, and coagulation time are essentially normal. Lastly, the total volume and viscosity of the blood are greatly increased, points of fundamental importance for the proper understanding of the clinical manifestations and the dangerous complications of the disease.

4.–CLINICAL PICTURE

Onset　　The onset is insidious: the patient may consult a doctor for one or any combination of the following symptoms: incapacity for work, lassitude, flushing, giddiness, sensations of throbbing in the head or headache, paraesthesiae or 'rheumatic' pains in the limbs. The appearance of the patient may give a clue to the diagnosis: the engorgement and stasis of the superficial capillaries are indicated in the exposed parts by a brick-red colour in warm weather, whereas cyanosis, often of a deep degree, is present in cold weather. The eyes may appear blood-shot, and ophthalmoscopic examination of the retinal vessels often reveals marked engorgement and dilatation; papilloedema may be present.

Nervous symptoms　　Symptoms referable to the nervous system are common: paraesthesiae of the limbs, insomnia, mild attacks of giddiness or loss of consciousness,

Gastro-intestinal symptoms　　weakness of the limbs, or psychical disorders may occur. Symptoms referable to the gastro-intestinal tract are often noted, particularly dyspepsia and constipation. Haemorrhages may occur anywhere, e.g.

Haemor-rhages　　in the nose, mouth, tongue, intestines, kidney, or brain. Thrombosis,

Thrombosis　　due to increased viscosity and diminished velocity of the blood, may cause a lesion in the brain, an infarct in the spleen, or a phlebitis in any

Blood-pressure　　situation. In many cases the blood-pressure may be normal for years, but in the later stages it is usually raised and arteriosclerosis is frequently present. Geisböck placed the cases of polycythaemia with hypertension but without splenomegaly in a separate category (polycythaemia hypertonica or Geisböck's disease), but there is little to recommend this classi-

Spleen　　fication. The spleen is usually palpable, but the degree of enlargement varies greatly in different cases and even in the same case from time to

time irrespective of treatment. It is firm and smooth to the touch and
may be tender if recent infarction has occurred. The liver may be *Liver*
moderately enlarged from engorgement. In the terminal stages it may
be shrunken from cirrhotic contraction.

Haemorrhages are the commonest complication. The patient may die *Complications*
from the extent of the haemorrhage or because of the damage produced
in important organs such as the brain. Disease of the blood-vessels may
lead to gangrene, Raynaud's disease, or erythromelalgia. Lastly, ery-
thraemia may occasionally terminate in leukaemia or, more rarely still,
in aplastic anaemia.

5.–COURSE AND PROGNOSIS

The disease is usually chronic and has probably been present for a long
time before the diagnosis is made. Spontaneous remissions lasting
months or years may occur without obvious cause. Although a cure can
seldom, if ever, be accomplished, the patient may live for ten to fifteen
years in reasonable health if suitably treated, but the risk of haemor-
rhage, heart failure, or intercurrent infection is always present.

6.–DIAGNOSIS

The diagnosis can be established only by finding the characteristic blood
picture after exclusion of conditions which cause secondary erythro-
cytosis. Ayerza's disease should only be diagnosed when dilatation of
the pulmonary artery can be demonstrated in the X-ray picture. A
positive Wassermann reaction would be additional evidence of value.
The cerebral manifestations and eye changes may simulate intracranial
disease.

The differential diagnosis from leukaemia may be very difficult in cases *Diagnosis*
showing many immature white cells in the peripheral blood. As already *from*
leukaemia
mentioned, some of these cases terminate in frank leukaemia.

7.–TREATMENT

Since the clinical manifestations of erythraemia are directly attributable *Symptomatic*
to increased blood-volume and increased blood viscosity, treatment *treatment*
must be directed to the relief of these features by reducing the number
of red blood-cells in the circulation. For this purpose many different
methods have been advised, most of which have proved ineffective. Thus
splenectomy is definitely contra-indicated. Benzene should not be used
because of its excessively toxic and depressant effect on the bone
marrow. Arsenic in large doses may be of some value and may be tried,
should the forms of treatment recommended below fail. The claims
regarding the value of splenic extract therapy have not been confirmed.

An entirely different type of treatment has been recently suggested, based on the hypothesis that the hyperplasia of the bone marrow in erythraemia is caused by an excessive production of a haematopoietic hormone in the stomach, the condition being the antithesis of pernicious anaemia, in which there is a failure in the production of the anti-anaemia factor. Accordingly a diet has been recommended in which articles of food rich in the extrinsic factor of Castle or in the preformed anti-anaemic factor should be reduced to the lowest possible quantities. Since erythraemia is a chronic disease, lasting for years, such a diet is unphysiological and impracticable. However, a moderate reduction in animal protein and the exclusion of foods rich in purines (liver, kidney, sweetbread) should be recommended, in view of the frequency with which a raised blood-pressure and its sequelae occur in erythraemia.

Choice of treatment There is a choice of three main methods of treatment: (i) venesection; (ii) irradiation with X-rays or radium; (iii) phenylhydrazine or its derivative, acetylphenylhydrazine. A combination of these methods may be used.

Venesection For venesection to be of any value a large quantity of blood must be withdrawn, since the blood-volume is often increased two- or three-fold. Little relief is likely to follow the withdrawal of less than forty ounces. There can be no doubt that venesection gives more rapid relief from subjective symptoms than any other form of treatment; its effect, however, is transitory, and it should not be used as the sole method of treatment, both for this reason and because it tends to stimulate the already hyperplastic marrow to increased activity. In an acute exacerbation of subjective symptoms, particularly if they suggest a liability to intra-

Technique cranial haemorrhage or thrombosis, it is the method of choice. Owing to the greatly increased viscosity of the blood, venesection is unlikely to be successfully accomplished unless certain modifications of the usual methods are used. (i) A wide-bore French's needle should be used, and the rubber connexion attached to this and leading to the receptacle for the blood should be as short as is consistent with convenience and thoroughly washed with citrate solution before use. (ii) When the vein has been selected the needle should be inserted in the direction opposite to that of the blood-stream. (iii) A vacuum should be maintained in the blood receptacle to hasten the rate of blood-flow through the tubing and so prevent clotting.

Irradiation The idea of applying 'stimulating' doses of X-rays to the spleen with a view to increasing the activity of the reticulo-endothelial system has now been abandoned in favour of depressant doses applied to the long bones, sternum, and ribs. Such treatment to be successful should be carried out carefully and controlled by repeated blood counts. If the dosage is too small, a stimulating effect on the already hyperplastic marrow may be produced; whereas, if too large, aplastic anaemia may result. Irradiation should not be applied to the head, in order to avoid alopecia, and in young people the pelvic bones should be omitted, to

avoid damage to the gonads. Pack and Craver suggested three to six exposures a week, until all the long bones had been irradiated. The course might be repeated at intervals of three to six months, depending on the response of the patient. They claimed that the general health was improved and life prolonged. It is probable that cases with a high platelet *Indications* count are particularly suitable for irradiation therapy rather than for phenylhydrazine treatment, since in such cases the tendency to thrombosis, already present, will be increased by treatment with the drug.

The effects of phenylhydrazine hydrochloride were carefully investi- *Phenyl-* gated by Giffin and Allen, who claimed that in thirteen out of fifteen *hydrazine* *hydrochloride* cases treated fairly good, good, or excellent results were obtained. The following features are held to contra-indicate treatment with phenyl- *Contra-* hydrazine: (i) age over 60; (ii) advanced arteriosclerosis; (iii) bedridden *indications* patients; (iv) patients with a history of thrombosis; (v) patients with definite disease of the liver or kidneys. It is essential that the drug should be freshly prepared. In the initial period of treatment patients should be in hospital, so that proper supervision may be carried out, but they should be ambulatory and may, in some cases, receive a course of massage in order to lessen the susceptibility to thrombosis. The dosage *Dosage* is 0·1 gram in capsules two or three times daily until 3 to 4 grams have been given, or until definite clinical evidence of active haemolysis (jaundice) occurs, if the amount necessary is less than this. The initial treatment usually lasts from ten to fourteen days. The drug should then be stopped, as the effect is cumulative and lasts for seven to ten days after its withdrawal. In cases which prove resistant, one or more courses of treatment, giving 0·1 gram twice daily for five days, may be prescribed at intervals of ten days. The maintenance treatment should be begun within a few weeks of the initial course. The amount necessary for maintenance of the blood count at approximately the normal level must be found by trial and error in each case; one to three doses of 0·1 gram on one day of each week is the average amount necessary. Long-continued treatment of this kind may occasionally be followed by a complete remission of the polycythaemic process for long periods. Thrombosis appears to be the main danger, and gastro-intestinal disturbances may cause some difficulty in administering the drug.

Acetylphenylhydrazine has been recommended by Stone, Harris, and *Acetylphenyl-* Bodansky, and by Rosenthal. It is preferred to phenylhydrazine because *hydrazine* it is practically as effective and less toxic, and the dosage is more readily controlled. The dosage is 0·1 gram once daily in a gelatin capsule for one or more courses of seven to ten days, during which the red-cell count should be carefully watched. For maintenance purposes 0·1 gram at intervals of five to seven days is approximately the amount necessary. Rosenthal found large amounts necessary in cases with initially high counts (about 10,000,000), e.g. 0·1 gram daily for three to five weeks.

For an emergency, venesection should be used. Irradiation appears to *Choice of* be of more general application than phenylhydrazine treatment, because *treatment* many cases are not suitable for treatment with the drug. On the other

hand, published reports appear to indicate that it is easier to keep the blood level about normal for long periods with the drug. A combination of phenylhydrazine and irradiation is recommended by Rosenthal for the leukaemoid group of cases.

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ERYTHRASMA

See FUNGOUS DISEASES, p. 469

ERYTHROBLASTAEMIA

See ANAEMIA, Vol. I, p. 462

ERYTHROCYANOSIS

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Reference may also be made to the following titles:

CHILBLAINS   RAYNAUD'S DISEASE
ERYTHEMA   SKIN TUBERCULOSIS

1.–DEFINITION

444.] The term erythrocyanosis is used to imply a reddish-blue or purple discoloration of the skin found chiefly in the lower half of the leg in young women of stout build. The lesion figures prominently in Continental literature under the cumbrous title of *erythrocyanosis crurum puellarum frigida.*

2.–AETIOLOGY

Although this description indicates its most common site, erythrocyanosis is occasionally found in other situations and may be encountered about the knee, over the tricipital area of the arm, and on the skin of the breast and buttock. It will be noted at once that the one factor common to these different areas is a tendency to excessive deposit of fat.

The thin, spare leg appears almost immune. Persons suffering from the *General* condition are of a stout and florid build with large limbs, in which the *appearance of patient* sturdy appearance is misleading and due to excessive fat. Their general

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appearance is that of rude health, and Mach, who gave a very good description of the lesion, stated that they excite no pity because they look so healthy. Descriptions of the disease in the male are rare and the few recorded instances have occurred on the buttocks.

The common case of erythrocyanosis then, is the stoutly built young woman who suffers from an area of purplish discoloration in the lower half of the leg, most evident in the region just above the malleoli (the *erythrocyanosis sus-malléolaire* of French writers).

Fig. 20.—Leucocytic infiltration of subcutaneous fat. ×150

The discoloration appears first only in the winter months and, beyond the subjective sensation of cold, causes no trouble. It tends, however, to become worse in succeeding winters and may fail to clear up entirely during the summer.

Theories of causation The aetiology is still obscure. The lesion is regarded by some authors as tuberculous and by others as due to endocrine dysfunction.

Tuberculosis There is no direct evidence that the condition is tuberculous. On the contrary, a number of unbroken nodules have been excised and have not produced tuberculosis in the guinea-pig. It is true that giant cells
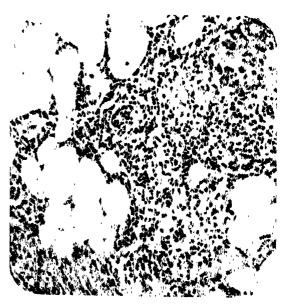
Fig. 21.—Further stage in process shown in Fig. 20; saponified fat being removed. ×150

are seen in sections of these nodules but these giant cells are not of tuberculous origin; they are, in fact, of the foreign-body type and are
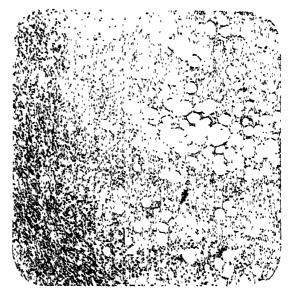
Erythrocyanosis in a woman aged 28 years. Attacks had occurred each winter
  for four years and ulceration developed shortly after exposure in a snow-
  storm. Healing took place in six weeks after lumbar cord ganglionectomy

PLATE III

packed with saponified fat. There can be no doubt that these cells have in the past misled certain less experienced observers. Stages in the evolution of the nodules are shown in the illustrations. Fig. 20 shows the early stage of cellular infiltration of the subcutaneous fat, and a further stage in the process is depicted in Fig. 21. Here the saponified fat is being removed and in Fig. 22 the process is nearing its end; the granulation tissue is seen developing into young fibrous tissue.

Endocrine dysfunction has been variously invoked as a cause and the *Endocrine* thyroid, parathyroid, ovarian, and pituitary glands have been incrimi- *dysfunction* nated. The literature on this subject is extensive but not convincing, and in a large personal experience I have found nothing to support the hypothesis of disordered internal secretion.

The explanation is probably to be sought locally, the essential factors being defective venous return, excessive fat, and the action of cold. On clinical and histological grounds the lesion is identical with the purple limb and the 'chilblains' of old-standing severe poliomyelitis.

Local conditions

FIG. 22.—Terminal stage; beginning of young fibrous tissue. × 50

Furthermore, on clinical features and histological appearances, the nodules of erythrocyanosis are identical with those of Bazin's disease, the tuberculous nature of which is, to say the least, very doubtful. The lesions of erythrocyanosis show a close analogy to those of 'fat necrosis'. It would, in fact, seem probable that all the above lesions have a common basis. Saponification of fat is the first event and the resulting nodule represents Nature's attempt at repair, which in some cases succeeds without ulceration but in other cases calls for the casting out of a slough.

3.—CLINICAL PICTURE

After two or three winters certain secondary changes are evident; the *Appearance* lower half of the leg, particularly its posterior surface, is of a purplish *of leg* hue which may be uniform or marked by scattered plaques of a deeper colour (see Plate III). The colour is blanched by pressure, but when the

pressure is released the area fills up quickly with dark blood from all sides in a way which Krogh has graphically likened to a subcutaneous lake of ink. The circumference of the limb is much increased by a firm elastic infiltration of the subcutaneous tissue. This may reach very considerable dimensions and may take the form of a thick and prominent cuff of tissue most evident just above the malleoli and shading off higher up the leg. It produces a clumsy and evident deformity. The appearance of the overlying skin is characteristic; it is stippled with small reddish points, in the centre of which is a minute keratinized focus. These are the hair-follicles enlarged and pigmented; the hair is usually absent, the 'kératose pilaire' of French authors.

Up to this point the resultant disability is trivial, the patient complaining only of the colour of the skin and the uncomely thickening above the ankles. In the more serious case, however, the condition

Nodules shows further complications. From time to time fairly large and very distinct indurated nodules appear in the subcutaneous tissue. When fully developed they are circular plaques 1 to 2 cm. in diameter, and are painful and tender. On inspection the overlying skin appears a little tense and reddened, and on palpation a definite discrete induration is found which spreads deeply into the subcutaneous tissue. Some patients say that they can forecast the appearance of these nodules by a severe itching long before they are apparent. The nodules undergo a slow resolution, which at the best occupies many weeks or even a whole winter. They often leave evidence of subcutaneous scarring and in one patient, a middle-aged woman who had suffered for many years, there was a large area of thin, fibrous skin in the lower half of the posterior aspect of each leg.

Ulceration She stated confidently that at no time had there been any ulceration. On the other hand, in a number of cases one or more of the nodules enlarges, becomes acutely inflamed, and finally bursts leaving a small circular ulcer in the base of which is a tough, adherent slough. These ulcerations are very slow to heal and often last until the beginning of summer. In the more severe cases sensations of weight and coldness in the leg, intolerable itching, and burning pain, together with the development of ulcers may render the patient quite unfit for any work.

4.–DIAGNOSIS

Erythrocyanosis must not be confused with acrocyanosis (*acro-asphyxie*). This latter condition affects the most peripheral parts of the circulation; its colour is darker and more leaden than is that of erythrocyanosis.

5.–TREATMENT

The common less severe case can be much improved by tonics, dietetic treatment to reduce fat, warmer clothing for the legs, and the use of a

supporting bandage. Hormone therapy of various kinds has proved of no avail, but some writers have claimed improvement after the use of calcium. In the more severe cases in which crippling and disability result from prolonged chilblains and ulceration, the use of a pressure dressing such as elastoplast may prove of value. For the more disabling and intractable forms, the operation of lumbar cord ganglionectomy has been performed and has been found to yield very satisfactory results.

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ERYTHRODERMIA DESQUAMATIVA

See ERYTHEMA, p. 173; *and* FOETUS DISEASES, p. 349

ERYTHROEDEMA

See PINK DISEASE

ERYTHROMELALGIA

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Reference may also be made to the following titles:

1.—DEFINITION

445.] Erythromelalgia is a condition in which one or more extremities are red, and are the source of burning pain which is induced by dependency and by warmth and is relieved by elevation and by cold.

Historical note
Under the title of 'a rare vaso-motor neurosis of the extremities' Weir Mitchell in 1878 collected five cases of his own and five described by others of the condition which he named erythromelalgia. Recent work leaves little doubt that, as illustrated by the cases of Weir Mitchell and others after him, erythromelalgia is not so much a disease as a symptom-complex expressing a certain state of the skin which may arise from several distinct causes. Some authors have attempted to separate from erythromelalgia those cases, such as those of obliterative vascular disease, in which the cause is known; but this is to ignore the pathological changes underlying the condition and to give a false sense of unity to the cases to which they would restrict the term. It seems that the name erythromelalgia must either disappear or must be used to describe cases

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presenting a certain group of phenomena irrespective of their ultimate causation.

2.–AETIOLOGY AND PATHOGENESIS

Any conception of the disturbance underlying erythromelalgia must account for its two characteristic features, the redness and the pain. The discoloration, often not very conspicuous in the horizontal position, is greatly increased by dependency, the skin at first becoming bright red and later more dusky. The characteristics of the pain have been mentioned in the definition. *Pathogenesis*

Lewis showed that the vascular and sensory phenomena of erythromelalgia occurred in skin which was in a certain phase of inflammation termed 'the susceptible state'. Lewis and Hess showed that, in normal subjects, this state might be induced temporarily in any part of the coverings of the body within a minute by burning, after several minutes by scarifying the skin or applying irritants, or after several hours by freezing the skin or exposing it to ultra-violet radiation. In diseased subjects this state may be exhibited as a chronic condition by patients suffering from obliterative vascular disease, from erythrocyanosis, from chronic chilblains, and from inflammatory states of the skin of more obscure causation. In such skin the minute vessels are dilated, presumably by the action of a substance or substances released from the injured cells; the skin is red, and it reddens further and then grows more dusky when the part is hung down, a colour change which is due to passive distension of the atonic minute vessels by the raised hydrostatic pressure of the blood in the dependent position. The skin is also peculiarly tender, burning pain arising from any interference which increases the tension in, or temperature of, the skin. Thus, the warm skin may be painless, but gently stretching it between the fingers, or distending it with blood by lowering the part, at once causes burning pain which subsides as soon as the tension is removed. Contact with bodies at 40° C., which gives a pleasant sensation of warmth in normal skin, produces burning pain in susceptible skin. Burning pain often arises 'spontaneously' in susceptible skin from vasodilatation, which increases both tension and temperature. The sensory phenomena of the susceptible state are also attributed to release of a natural chemical substance from the injured cells of the skin. Usually the rate of release of this substance is inadequate directly to stimulate the pain-nerve endings but lowers their threshold to stimuli such as tension and temperature. Further injury of the cells appears to increase the rate of release of this substance, with the result that its concentration may rise above the threshold for stimulating the sensory fibres; thus rubbing the skin for a few seconds may produce pain lasting several minutes; the chemical origin of this pain is shown by its delayed disappearance when the circulation to the limb is arrested. *Lewis's explanation of pathogenesis*

Lewis pointed out that, since this susceptible state might and did occur

in any part of the skin, it was more properly termed erythralgia than erythromelalgia.

Until Lewis's work erythromelalgia was generally considered to be a vasomotor neurosis, a conception due originally to Weir Mitchell. Mitchell was much impressed with the pain and reddening on dependency. The colour change, which, as has been shown, may be explained on mechanical grounds, was regarded by Mitchell as due to a 'vascular storm', a sudden active vasodilatation brought about reflexly through the vasomotor nerves. In support of this he stated that, in a typical case, when the foot was lowered the arteries would throb violently for a time and the foot would become hot; these two statements have been repeated in most descriptions of erythromelalgia, but critical examination of the case records of Mitchell and others shows that they are made on inadequate evidence. On the basis of Lewis's work, vasodilatation may be expected to produce pain in the abnormal skin of erythromelalgia by warming and distending it; there is no evidence that in erythromelalgia arterial dilatation occurs in abnormal circumstances, or to an abnormal extent, or is especially associated with the dependent position. The vasomotor hypothesis is unnecessary to explain the vascular and has never explained the sensory phenomena of erythromelalgia, and is entirely excluded by the failure of sympathetic ganglionectomy to cure the condition in some cases in which it has been used.

Aetiology

The work just described indicates that the symptom-complex of erythralgia or erythromelalgia is a manifestation of an inflammatory state of the skin. It may be anticipated that, although the factors bringing about this state will differ in different cases, they will in general be such

Causal factors as injure the skin. Among the factors recognized are:

Obliterative vascular disease

(a) Obliterative vascular disease. This presumably acts by reducing the blood-flow to the skin, which is thereby under-nourished and disposed to injury by cold and other agents. In Weir Mitchell and Spiller's patient, a man of sixty-one, the pulse was absent below the groin in the affected right leg, and the arterial lumen was grossly reduced by intimal thickening in the amputated great toe. Several of the cases described by Sachs appear to have been cases of thrombo-angiitis obliterans, in which disease the symptom-complex is not uncommon. One of Lewis's patients had thrombo-angiitis and another degenerative arterial disease. Other cases, in which obliterative vascular disease was present, are mentioned in Barlow's article.

Cold

(b) Injury by cold. Lewis had two patients with erythrocyanosis of the legs and one with chronic chilblain of the foot. The condition has followed frost-bite.

Mechanical injury

(c) Mechanical injury. In one of Mitchell's cases the complaint appeared in the hand after prolonged use of a geological hammer; in another it started in the foot after injury by a block of stone weighing half a ton, and in a third after a severe wrench of the foot. The complaint has also followed prolonged standing or walking.

(d) Bacterial injury. In Bradford's case and one of Barlow's the com-

plaint followed injury to the hand succeeded by swelling which required *Bacterial*
incision. To what extent bacterial injury contributed in these cases is *injury*
uncertain. I have experienced the symptom-complex of erythromelalgia
for a short time in my own foot, during a superficial widespread pyo-
genic affection of the skin following an infected burn.

In most cases, however, the causation is obscure; in some the condition
has followed debilitating fevers, and in others it appears to have been
associated with disease of the central nervous system; in one of Lewis's
cases it was accompanied by a peculiar form of factitious urticaria in
which whealing was accompanied not only by the customary itching
but also by burning pain. Even in those cases in which there is a clear
history of injury this cannot be the only factor, for injury is common
and erythromelalgia comparatively rare; moreover, the susceptible state
following experimental injury is transient, whereas the clinical condition
erythromelalgia persists.

3.–SYMPTOMS AND SIGNS

In the description of the clinical manifestations of erythromelalgia atten-
tion will be restricted to those phenomena properly belonging to this
condition; other phenomena which may arise from the causal disease,
for example obliterative vascular disease, will not be mentioned.

The initial complaint is of pain which is described as burning, stinging, *Pain*
or smarting, and is often localized to a small area of skin in a lower, or
less commonly in an upper, extremity. The pain is at first experienced
only at intervals; in the lower extremities it comes after prolonged
walking or standing. As the disease progresses, the area involved be-
comes greater and the pain more easily provoked. Anything which rubs
the skin, causes congestion or warms it, produces pain. Thus walking
produces severe pain and in bad cases may be impossible, the patient
crawling on his hands and knees or having to be carried about. Putting
the foot to the ground may be enough to produce intolerable agony.
The part is only comfortable if it is elevated and then only if cool. The
warmth of the bed-clothes may provoke pain, and patients often sleep
at night with the part uncovered or covered with only a thin sheet;
during the day a low shoe is preferred to a heavy boot, and some have
refused to wear socks or have insisted on keeping their feet bare. The
part is washed in cool or tepid but not in hot water. The complaint is
often more severe in summer than in winter.

On examination in the horizontal position the affected skin is highly *Appearance*
coloured, may be somewhat swollen or indurated, and may be shiny; *of affected*
sweating is sometimes excessive. The part may be warmer or cooler than *limb*
normal or than the corresponding unaffected area on the other limb.
On lowering the limb the colour quickly deepens, the tint remaining
bright at first and then gradually becoming dusky; the temperature
remains more or less unchanged or may fall a little. On return to the

horizontal the part resumes its usual colour. The affected skin is tender to the touch and gives rise to burning pain when rubbed, congested, or warmed as previously described. Otherwise sensation is normal. Arterial pulsation may be present or, in obliterative vascular disease, absent.

Parts affected

The condition, as has been remarked, usually begins in one, commonly a lower, extremity. It may remain confined to this or may eventually involve one or all of the remaining limbs. More rarely the condition affects the skin of the trunk.

4.—DIAGNOSIS

Diagnosis from causalgia

Redness and burning pain with the characteristics defined are associated only in erythromelalgia and so-called causalgia. Causalgia, however, always results from injury to one of the peripheral nerves, of which evidence can usually be easily obtained. Diagnosis in erythromelalgia consists chiefly in determining, when possible, the underlying disease. In view of its common occurrence, tests for obliterative vascular disease should be made in all cases.

From erythromelia

Erythromelalgia should also be distinguished from erythromelia, a painless progressive affection in which red areas appear and spread in a centripetal manner on the extensor aspects of the legs or arms.

5.—PROGNOSIS

Prognosis is always uncertain and often bad. Early cases have remained stationary, and bad cases have recovered; but the condition is notoriously refractory to treatment. The condition itself never proves fatal, but prolonged and severe pain too often leads to mental and moral deterioration and suicide.

6.—TREATMENT

An effort should always be made to discover and remove causal factors. In cases in which the condition is due to exposure to cold adequate protection by clothing should be ensured. In cases due to arterial disease measures should be taken to increase the circulation.

Sympath-ectomy

Sympathectomy appears to have produced pronounced improvement in carefully selected cases of obliterative arterial disease; it might also be expected to improve cases in which the disturbance is due to erythro-cyanosis or chilblains; but such cases are rarely sufficiently intractable to justify the operative risk; in cases in which the susceptible state cannot be clearly attributed to deficient blood-supply sympathectomy does not improve, and may aggravate, the condition.

General treatment

In many cases the causal factors are unknown or cannot be removed, and general measures, of which the cardinal principle is rest, must be

used. The affected extremity is kept elevated and as warm as is consistent with comfort; the joints should be kept supple by active or passive movement. Analgesics must be administered cautiously to avoid habit formation. Local applications are of doubtful value. In mild cases persistence with such measures may arrest or cure the condition; but advanced cases too often remain refractory, and pain can only be relieved by nerve section or by amputation. When considering amputa- *Amputation* tion it is well to recognize on the one hand that some cases eventually undergo spontaneous cure, and on the other the severe mental and moral consequences of prolonged inactivity and intolerable pain.

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ERYTHROMELIA

See ERYTHROMELALGIA, p. 192

ESPUNDIA

See LEISHMANIASIS, CUTANEOUS

ETIQUETTE AND ETHICS IN MEDICAL PRACTICE

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1.–INTRODUCTION

446.] The practice of medicine brings to those who serve it contacts with patients, with colleagues, and, on occasion, with public opinion and public interests. In each of these relations the practitioner has more or less often to face situations not always free from difficulty. As a

result there has gradually accumulated a body of experience upon which *Basis of medical ethics* are based certain conclusions and counsels that have come to be named, somewhat loosely, medical ethics and etiquette. The term has an imposing quality and in the popular judgement is often given a significance and severity that it does not actually possess. The suggestion in this mistaken interpretation is that in order to maintain a professional status and a corporate loyalty doctors accept and apply a formal and rigid code which puts the interests of the profession, real or supposed, in the first place, and the interests of the public, or even of the patient, at a subordinate level. To the medical reader such a proposition is little short of an absurdity. The fancied formalities and regulations, imposed by authority and claiming penalties for their neglect, simply do not exist. In the nature of things there are customs and fashions which are seemly among those engaged in one and the same profession and well aware, as outsiders cannot be, of the special difficulties which attend their common occupation. But in no degree or instance are these *Governing principles in professional code* observances prior either to the welfare of the individual patient or to the general interest of the community. On the contrary, the first and commanding article in the professional code is recognition of responsibility to the patient, and no demand or influence or consideration can take precedence of this duty. Between members of the same profession there will, of course, be cultivated the ordinary courtesies of civilized society and some measure of a good fellowship born of common sympathies and an experience of common difficulties. Nor is this position impaired by a degree of healthy and not ungenerous rivalry, which, indeed, is to the advantage alike both of the public and the profession. Quite emphatically, however, medical practitioners are not mere students of popular favour and commercial success. Rather are they engaged in a serious profession which finds its justification in the service of sick folk and in the promotion of personal and communal health. Although in the pursuit of these ends medical practitioners have, and justifiably, their own methods of procedure, they are neither bound nor compelled by any ritual or regulation which prevents them as free men from the endeavour to meet the needs of those who in full confidence apply to them for assistance and advice.

To state these propositions is to recognize that professional activities *Medical etiquette and public opinion* and fashions, as included in the claim of social service, must be prepared to make their plea in the court of public opinion; and indeed, to this tribunal the profession and its ways are often summoned, whether the doctors like it or not. It follows that every member of the profession should be prepared to present an effective justification of professional procedure, whether this be regarded as a mere domestic custom or as an expression of general policy. Chapters and indeed volumes have been written on the subject of medical ethics, but none of these fails to emphasize what is here stated, namely, that the claim of the patient is always the first consideration and that medical policy is consistently and steadily directed to the interests and well-being of the community.

It has been argued that, as the medical practitioner is drawn in one
direction by the temptations of his own pocket and in the opposite
direction by the interests of the patient, he must needs succumb to the
selfish motive. This, manifestly, is to reason in the air; a certain propensity
of human nature is assumed to exist in isolation, and from this is deduced
an inevitable consequence. The parallel argument would be that as an
absolute monarch is all-powerful he is certain to rob all his rich subjects
and to cut off the heads of everyone who annoys him. Motives and de-
cisions in practical life are, however, not quite so simple as this reason-
ing implies. To suggest that as doctors have a pecuniary interest in human
ills they cannot cultivate a sincere effort to lessen these is just as true
and just as untrue as to insist that judges cannot desire to lessen liti-
gation, or soldiers war, or policemen crime, or clergymen impiety. What
determines conduct is the situation actually existing, not some vague
and remote ambition, and the situation presented to the doctor admits
only two possibilities. The one is to take advantage of ignorance and
helplessness and emotional susceptibility for his own selfish advantage,
and the other is to follow natural decent human instincts, to respond
to professional tradition, and to cultivate the pride and responsibility
of craftsmanship. The choice is a simple one, and the doctor makes
it untouched by any degree of philosophic doubt and unaware indeed
that the issue is open to debate.

2.—INTRA-PROFESSIONAL RELATIONS

447.] Although many practitioners, probably the majority, hardly need
specific guidance or instruction on their relations to their immediate col-
leagues, other than the classical precept of the golden rule, circumstances
do sometimes arise which make intra-professional relations strained or
even contentious. With a sense of good fellowship, a recognition of
common difficulties, and the practice of frankness, most disputes can be
resolved; and in the effort to this end the personal interview is much to
be commended rather than the dexterities of controversial correspond-
ence, and open discussion rather than the private nurture of bitterness
and resentment. Letter-writing, not always avoidable, is apt to sharpen
the temper as well as the pen. On occasion, however, and even in spite
of goodwill, some acute issue will arise with perhaps something to be

*Mediation in
intra-
professional
disputes*
said on each side. Such a situation is one for an impartial judgement,
and if some senior and trusted practitioner cannot be found for the
task the services of the local Division of the British Medical Associa-
tion or of the Association's Central Ethical Committee may advisedly be
requested. Many experiences show that understandings can often in this
way be resolved, and when error is found, a frank recognition of it will
go far to redeem the situation.

*The
traditional
code*
Of course there are defined rules which govern individual positions and
circumstances, but for the most part the commanding influence is a body

of tradition reached after trial and error and embodying what in common regard is spoken of as fair play, loyalty, and the spirit of the game, as these qualities appeal to those who are engaged in one and the same calling, share the same responsibilities. and are liable to the same risk of misinterpretation. Practitioners are agreed that the patient's claim is their first care: they recognize a common ideal; for none of them is the road always easy; and ignorant and unfair judgements few may escape. Well therefore may they cultivate a mutual loyalty and even a measure of charity. And not without importance, be it noted that quarrels and hostility between neighbouring practitioners are not agencies which promote for the profession the respect and regard of a public which, though not uncritical, is also not ungenerous.

3.–THE SECOND OPINION

448.] Among the events which sometimes disturb peaceful intra-professional relations and cause friction between colleagues is that created by the desire of the patient or of his friends for a second or further expert opinion. And here it must be remembered that quite naturally voices other than the voice of the doctor claim to be heard. Nor can the claim be denied. Indeed it must in principle be allowed to be not unreasonable, for the patient is the figure most concerned in the drama, and he surely has a right to everything which he believes, whether on adequate or inadequate grounds, may contribute to his recovery. For the most part *Patient's* an attending practitioner will welcome the co-operation of a colleague, *rights in choice of* but whether he approves the proposal or not, the final word is not with *consultant* him. He may offer his opinion both on the wisdom of the proposed course and on the source from which a second opinion, if it is desired, should be obtained. But neither on the one point nor on the other is he entitled to dictate, or to take offence should the patient prefer to make his own choice. The sick man has, in short, the rights of the situation. Sometimes he exercises these rights without the knowledge or consent of his usual medical adviser, and in so doing he probably acts unwisely, and certainly with some failure of courtesy. It is not unnatural that the doctor should resent this action. Yet judgement must not be unduly severe. A patient anxious about his health and future may well be excused some deficiency in the social graces, and even some want of consideration for professional dignity and susceptibility; and the wise practitioner in these circumstances, as in others, cultivates the value of the equal mind. That the second doctor would probably be a more useful guide had he the earlier and particular knowledge possessed by the first attending practitioner is obvious enough to the professional eye, but not necessarily to the eye of the patient who desires what seems to him an 'independent' opinion.

Sometimes in professional circles the right of a second doctor to examine a patient already under medical care and to give this 'inde-

pendent* opinion is challenged. In its broadest form this would mean that a patient could never obtain a second opinion except with the willing co-operation of his usual doctor, and such a position, whatever the medical profession might say about it, could not possibly hope for the sanction of public opinion. And obviously, if the right of the patient to seek such opinion is allowed, his right to obtain and receive it can hardly be questioned. The patient is not the property or possession of any doctor, and doctors exist for his interest, not he for theirs. Similarly it is open to any patient at any time to change his medical adviser if for any reason, or indeed without a reason, he desires so to do. And a practitioner, in turn, may well desire to be freed from professional responsibility when this is not associated with a responsive confidence and loyalty.

Intra-professional duties of second doctor
If, however, as is here allowed, a patient may, however unwisely, elect, without his doctor's knowledge, to obtain a further professional opinion on his case, there does arise a position which presents emphatically a claim for intra-professional courtesy. This is that the second doctor shall obtain the patient's permission to communicate with the original attendant, and shall, unless this permission is granted, refuse to take the patient under his professional care. The defence of this position rests on two considerations. The first is that when two doctors are concerned with one and the same patient it is in the interests of the patient that they act in co-operation. The second is, that if responsibility is to be transferred from one adviser to another this should be done openly and frankly and with due courtesy to the doctor who ceases to direct the therapeutic measures required. There is no proposal to limit the patient in the choice of his medical adviser or to hinder by formalities the exercise of this choice. Hence if co-operation between the doctors concerned is not desired, the patient's will is law. All that can be asked in such circumstances is that to the retiring practitioner shall be conveyed a courteous intimation of the position and that the practitioner with whom the responsibility is in future to rest shall receive full recognition and authority. These considerations apply whether the practitioners concerned are engaged in family practice or, mainly or entirely, in consulting practice. The opposition suggested by these terms is indeed in advance of the facts. While it is true that in large towns there are practitioners of established position who confine themselves to limited branches of practice and to consultations in the technical sense of this term, both here and in other areas family or general practitioners of senior position and recognized repute are often asked for co-operation by their colleagues, to the great advantage both of medicine and of the community. It would not be consistent with the free atmosphere of medicine to limit consulting practice, or indeed any form of practice, by hard definitions and restrictions, nor would such a policy command either public approval or the public interest.

4.–PROFESSIONAL CONFIDENCES

449.] To the patient the doctor owes, of course, his best service and *Reasons for* advice. This is the contract implied in the relation between doctor and *professional secrecy* patient. Not less emphatic is the demand that the doctor shall scrupu- lously respect his patient's confidence. Here indeed is the basis on which they meet, and it is easy to show that a full regard to the claim is a large public interest as well as a bond due to the individual patient. Unless it is observed patients will be inclined to avoid medical advice so long as postponement is possible, and hence the early and curable stages of illness will escape their best opportunity, while in the case of infectious disease the chances of extension to other persons will be multiplied: the proverbial stitch in time may be missed, and risks to others may be increased. Further, with the absence of secrecy, frank and free disclosure by the patient will be discouraged, and the doctor in corresponding measure will be imperfectly informed for his task. To betray confidences is in the nature of things a shameful and dishonourable act. But, in addition, as is claimed here, silence by the doctor relative to his patient and his patient's affairs has the endorsement of the public advantage.

There are certain influences which tend to invade and loosen this bond. Kindly inquiries by relatives and friends may be well intentioned and apparently harmless. The proper direction for such inquiries, however, is not to the patient's doctor but to the patient's friends. There are, for some, graceful and tactful methods of presenting this proposition, and a rival inquiry directed to the inquirer's own interests may some- times avoid the difficulty. In any event it is no bad reputation for a doctor to be known as one who never talks about his patients, and certainly to this practitioner never come the risks which on occasion fall upon the good-natured and the communicative. Better be gruff than garrulous.

This rule of silence should be rigidly and invariably applied to inquiries *Inviolability* taking origin from solicitors, insurance companies, employers, business *of rule of* partners, and others having a possible financial interest or responsibility *silence* relative to the patient. If the patient authorizes disclosures, preferably in writing, the rule obviously does not apply. But apart from such consent refusal should be absolute, and indeed it is well to remember that betrayal of information received in the consulting-room or at the bedside, and to the patient's prejudice, may be the motive for a success- ful action at law with, as a result, a penalty of substantial damages.

Now and again the argument is advanced that the doctor ought to supply, or even to volunteer, information regarding his patient when it would seem possible that such disclosure might prevent an unfortunate marriage or other mischievous event. But if exceptions to the obligation of secrecy are to be allowed, where are they to stop? No doubt the position created by an arranged marriage is an appealing one, but can the appeal be limited to one particular class of disease? If a function

of the medical profession is to be alert to use confidential information
for the supervision or control of contemplated marriages, why halt at
communicable disease? May not intending brides and bridegrooms
equally urge that the practitioner should, as opportunity offers, inter-
vene also to protect them from an epileptic, a tuberculous, or an insane
partner, or from one whose personal history or family record shows a
decided tendency to any one of these diseases? Again, why limit the
protection to intending brides and bridegrooms? Are there not others,
equally deserving, who make contracts—social, financial, sentimental—
in which health is a large factor, or who are well within the zone of
possible infection? The plea for disclosure in such circumstances is the
more without warrant seeing that the persons concerned have already
a full opportunity for self-protection. All that is necessary is that each
party to the contract should demand from his contemplated partner a
satisfactory medical certificate, which, in the case of marriage at least,
might well include some family details. Inquiries about the bank-book
offend no one's delicacy, why should the health record be treated with
timidity? The doctor, be it remembered, is a healer of sick folk, not a
judge of morals or the executive officer of an ethical code. Having
received his patient's confidence he is bound to treat this with a full
measure of reserve. With communicable disease in question he will of
course warn his patient of the danger, and even of the wickedness, of
certain actions. But to proceed to offer information to possibly inter-
ested persons outside the consulting-room is both a breach of trust and,
in addition, a prejudice to the common interest by weakening the public
faith in the trustworthiness of the medical profession.

Admittedly there are now and again difficult and delicate situations,
as for example communications to a husband or a wife relative to a
matrimonial partner's illness, but even here the presumption is for
silence unless the patient authorizes disclosure. There may on occasion
be a debate within the court of conscience, and no one proposes that
the doctor should tell other than the truth. But is he bound to tell the
whole truth? The question, in principle, frequently arises in reference to
answers to be given to the patient himself, who surely should be told
only so much as it is in his interest to know; and this doctrine may
equally be applied to others, if any, entitled to information. The situa-
tion, too, is in some measure relieved by the consideration that it is the
purpose of medicine to give the patient sound therapeutic and pro-
tective advice, not to accumulate pathological phrases in the popular
vocabulary. The patient often demands a diagnosis; what he needs
is a scheme of treatment.

*Protection
by medical
defence
organizations*   In these and other difficulties that may occur in practice it is a great
advantage to the practitioner to be a member of one or other of the
medical defence organizations. For a modest annual subscription he
can obtain experienced advice in any emergency and legal aid in
any action for damages in which he is made a defendant. Unfounded
accusations and attempts at blackmail are definite risks in medical

practice, and it is elementary prudence to be forearmed against them. Security and mental comfort lie with protective membership, the risk of serious trouble with neglect; and the wise practitioner waits not for the emergency but anticipates this by an immediate subscription.

5.—PROFESSIONAL CONFIDENCES AND THE LAW

450.] On the subject of medical confidences the Law has its own important word. On the one side it may penalize the practitioner who betrays them: on the other it will demand their revelation on behalf of what it deems to be the general good. This latter position is illustrated by the compulsion of the medical practitioner to certify the cause of death, to communicate to the appropriate authorities cases of certain diseases, infectious or industrial, and, directly or indirectly, to register the fact of birth. In all these issues there is no contest: what the law declares the loyal citizen obeys. There is, however, one situation where the legal demand is not without at least a shade of doubt. This is the witness-box. As a matter of legal doctrine there is in this respect no difference between *Medical* the medical witness and any other witness. He, like his fellows, must *witness* suffer and answer any question put to him unless this is disallowed by the Court. He may plead the bond of professional honour and may request protection, but if the Judge is against him on the point he must either answer or go to prison. If his protest is disregarded—and it is not always disregarded—he may perhaps find comfort in the reflection that the responsibility rests not with himself but with the law, and it may be that some day a practitioner may elect for the heroic course in defence of what has been named 'medical privilege', though the claim for this is *'Medical* obviously made in the interest not of the practitioner but of the patient. *privilege'* The only 'privilege' recognized in the witness-box is that of the solicitor, who, for manifest reasons, cannot be asked questions relative to communications made to him by his client. Neither the consulting-room nor the confessional is in this position. In practice, however, the priest enjoys security because the Court knows that even under the threat of prison he will not reveal the secrets of his penitent. As a contrast, the medical witness hitherto has found the pathway of verbal protest the less arduous choice.

The executive officers of the law, that is, the police, show at times a defective appreciation of the public value of professional confidences, and in their quite proper zeal in the detection of crime sometimes address to doctors questions in relation either to individual patients or to general experiences which should be approached with much reserve. If the doctor is summoned as a witness the position is as already stated, but outside the witness-box the presumption is in favour of silence. It is well that crime should be detected, but it is well also that medical confidences should be respected, and a fair statement of the position is that

whereas neither doctors nor any other good citizens will take part in the concealment of manifest crime, it is no part of the duty of medical practitioners to appraise the significance of admitted or alleged facts, or to repeat hearsay statements, or to act as agents of the detective police.

Doctor's duty in criminal cases

An acute position arises when the patient appears to be dying as the result of some criminal act, e.g. poisoning, or an illegal operation, or criminal neglect, or starvation. As the doctor in attendance will not be able to give a death certificate, there is bound to be a legal inquiry, and secrecy is obviously both impossible and undesirable. Moreover, the law provides that in such circumstances the patient should be given the opportunity of making a deposition before a magistrate, and a communication to the authorities must be made to secure this; or, if time presses, the doctor himself must be prepared to take down from the patient a 'dying declaration' under certain definite conditions as defined in the text-books. Here indeed the medical practitioner acts, and quite properly, not merely as a confidential adviser of his patient but as a citizen who follows the course which in the circumstances the law prescribes. The position thus presented is quite different from one in which the patient is making a satisfactory convalescence and none but ambiguous circumstances suggest that perhaps somewhere in the background there may have been illegal action. The first claim on the doctor here is the medical protection of the patient, not the investigation of possible moral or legal delinquencies.

6.–ADVERTISEMENT

General Medical Council's interpretation

451.] On one subject the medical profession is held definitely by an entirely rigid rule and the risk of a correspondingly severe penalty. The rule is directed against personal advertisement, and the interpretation given to this term by the General Medical Council is advertising, whether directly or indirectly, by a registered medical practitioner, for the purpose of obtaining patients or promoting his own professional advantage; or procuring or sanctioning or acquiescing in the publication of notices commending or drawing attention to the practitioner's professional skill, knowledge, services, or qualifications. And the penalty on proof of the facts is removal from the Medical Register.

It may confidently be claimed that the rule enjoys the support of the profession and generally of educated public opinion. The practice of medicine is not a business enterprise, and its status and influence will not be promoted by business methods. A rival display of qualifications and accomplishments would confuse rather than enlighten a public unacquainted with the exact significance of technical diplomas; and invitations and emphasis in the market-place could hardly be reconciled with a professional conscience at least as aware of limitations and doubts as of possibilities and achievements. Thus the advertisement column as an

avenue to popular favour is emphatically forbidden ground, and few indeed must be the practitioners who regret the restriction.

Less easily defined is the interpretation of 'indirect advertisement', *Indirect* which equally comes under the censure of the General Medical Council. *advertisement* The judgement here is directed to motive, and the question to be answered is, Is the performance, whatever it be, an effort to attract patients or to promote the practitioner's professional advantage? While the estimation of motive carries admitted difficulties, it is certain that the restriction, such as it is, is not directed against activities which are the common right of free citizens in a free State; these, doctors share with their fellows. Still less is the purpose, as is sometimes suggested, to keep the public ignorant of the laws of health, of the methods of preventing disease, or of the imagined secrets and mysteries of the medical profession. As for the last mentioned they simply do not exist, and the art of medicine, which may be fairly defined as common sense based upon scientific knowledge and practical experience, will be aided, not hindered, by the co-operation of an educated and enlightened public opinion. If the practitioner by his personal effort can contribute to such education, he is serving alike both his profession and the general community. There is no ground whatever for the suggestion that he is forbidden to publish articles in lay newspapers, or to write letters to the editor, or to deliver lectures to public audiences; and this is true whether his text is a professional or a non-professional topic. Indeed, such intervention in public affairs may on occasion, and in consequence of his knowledge and influence, be part of the civic duty of the practitioner. At the same time these tasks must be undertaken with discretion; must be marked by the motive of public service, not by that of personal ambition; and must be conducted with due regard for professional reserve and seemliness. An entrance on the newspaper scene heralded by a puff preliminary in the shape of a laudatory editorial preface and accompanied by a wealth of technical titles and decorations, a personal photograph, and a professional address, is likely to raise a doubt in the minds even of the unsophisticated as to the real ambition of the performance. The rule for those who undertake these activities, if they would escape misconstruction, is to avoid even the appearance of evil and to practise a due suppression of the personal note.

Comment sometimes arises on the appearance of professional names *Press* and activities in the 'social' columns of certain newspapers, and it is *publicity* beyond question that some of these are secured by the payment of a more or less considerable fee. Manifestly, if paid announcements in the advertisement column deserve censure, paid announcements in the social column cannot be approved. Yet on an appearance in these select companies judgement must not be too swift or too censorious. Fame has its penalties and editors have their fashions. What is judged by the journalist to be of interest to his readers will receive publicity whether the victim approves or disapproves, and whether professional colleagues criticise or applaud. An announcement which on the face of it may read

as a personal invitation to popular recognition may in fact be merely
the enterprise of a reporter anxious to enliven his columns. Less easy
is it to find a consistent defence for the record of personal and pro-
fessional achievements duly chronicled in the annual issue of certain
reference volumes which enjoy a considerable social vogue, for here,
admittedly, greatness is not thrust on the hero; on the contrary, the
record of his achievements is contributed by himself. Presumably
the story engages some degree of public interest, and the practice seems
to have the sanction of custom and habit. A comment from a non-
medical writer reads: 'The public as it turns the book over is not
deceived. It distinguishes, by an instinct of its own, between the publicity
which is enforced upon greatness and the self-advertisement of the
microcosmic.'

Quite naturally and properly the medical profession generally in view
of its status and creed is sensitive in the matter of personal advertisement,
but this attitude does not imply any limitation of the rights and oppor-
tunities of citizenship, nor an attempt to dictate to the Press, the discre-
tion of which on any particular occasion is, in its turn, always open
to comment.

7.—UNQUALIFIED PRACTICE

The legal position

452.] This is a subject on which the medical profession now and again
suffers challenge from the public. And the challenge must be frankly
met. In accord with the law of the land any citizen who wishes to do so
may give either medical or surgical advice, and may apply, on his own
responsibility, either medical or surgical treatment; and, similarly, any
citizen who desires such advice or treatment may seek it from any source
which commends itself to his judgement. The law, however, also says
that persons who have received a certain technical training and have
passed successfully certain examination tests may be registered as
qualified medical practitioners and may apply to themselves correspond-
ing titles, whereas those who have not satisfied the prescribed conditions
may not call themselves by these titles. In short, the law regards it as
necessary in the common interest that members of the public shall be
able readily and certainly to distinguish practitioners who have been
adequately trained and examined from others who have not suffered
this discipline; and it leaves the individual citizen to make his own

Attitude of medical profession

choice. Qualified medical practitioners alone have the right to distinctive
medical titles, but they have no right to a monopoly of medical or
surgical practice. With this legal position the medical profession has
no quarrel, provided that those who are not qualified do not attempt
to deceive the public by pretending that they are qualified, and provided
also that, as is necessarily the case, both parties to the transaction
accept the responsibility implied in their respective decisions. At the
same time the medical profession is bound to maintain that for the safe
practice of the difficult and responsible art of medicine and surgery

training in fundamental principles is an essential condition, and common sense endorses the claim. Doctors, like lawyers, architects, and engineers, are not born; they are made. And they are made by a curriculum which instructs them in the scientific basis of medical practice and in the practical problems presented by sick and suffering men and women and children in hospital wards and out-patient clinics. Skill, judgement, and efficiency, here as elsewhere, are obtained only by training and discipline and experience, and they are needed both to recognize the evidence of disease and, a not less responsible task, to certify its absence. Hence, while the medical profession desires neither to compel nor to hinder any man, it cannot accept the proposition that it is either safe or prudent for the sick man, whatever be the form or degree of his complaints, to accept either medical or surgical treatment based on a diagnosis suggested by anyone who has not been educated and trained in accordance with the demands of the medical curriculum and the hospital experiences which this includes.

That such a course is sometimes adopted without harm and even with benefit may be true, but the result does not prove either the absence of risk or the wisdom of the choice, and the medical profession accepts responsibility neither for the one nor for the other. With this it is freely allowed, and indeed welcomed, that particular methods of treatment, physical, electrical, balneological and the rest, may be usefully and effectively applied by persons trained for these ends and without medical qualification. But prior to treatment of any kind is the need for diagnosis—the identification and interpretation of the signs of disease with a view to determine what forms of treatment may properly be applied. And for this large and responsible task nothing less than the medical curriculum suffices. The plain statement is that only on the basis of scientific knowledge and a carefully garnered clinical experience can the safe and successful practice of medicine securely rest. And it is a public interest to mark a clear distinction between those who have, and those who have not, received this training.

8.—NEW REMEDIES

453.] As of books, so of remedies; of the making of them there is no end. Not a few proposals of this order take origin outside the ranks of the medical profession, and though the fashion of the amateur therapeutic world often passeth away, this does not mean that it should receive no consideration. The attitude of medicine to such proposals may be briefly stated. It is necessarily the desire and the duty of the medical *Duties of* profession to regard with attention any method suggested for the treat- *medical* ment of disease from whatever source this may take origin, provided *profession* that there is either scientific or empirical evidence which justifies some degree of reasonable expectation that the method proposed may prove beneficial and is not likely to do harm to the patient. Equally it is the

duty of the medical profession to refuse to spend time in applying experimentally to sick folk methods or substances which are destitute of adequate presumptive evidence in their favour. Doctors, being fallible, may on occasion put into the second of these classes something which might have been put into the first. On the other hand, they are aware of a long series of popular enthusiasms and confident claims upon which time and experience have passed an adverse verdict, and to put aside what has proved to be at least of some value for a novel and more or less speculative scheme of treatment can hardly be justified in the interests of the patient. Therapeutic wonders are not impossible. But

Doctor's freedom of choice

they are rare, and the improbable is not a safe guide either for life or for medical practice. The medical profession will in principle close its mind to no proposal, but equally it will not neglect its responsibilities for the sake of what may prove, and indeed often has proved, a mere passing fashion without warrant or foundation. The medical practitioner is a free man with the right, and with the duty, to use whatever method of treatment he judges to be in the interests of his patient. No code or college or council pretends to compel him to a statutory or 'orthodox' method or standard. The needs of the bedside must be judged by the practitioner himself, and he alone can conclude what these require. This he is free to do, and with the freedom goes in corresponding measure the burden of responsibility.

9.–CONCLUSION

454.] Compared with the serious responsibilities of medical and surgical practice the subject of medical ethics and etiquette may seem of small importance. Yet it cannot be safely or wisely neglected. At some points it touches the demands of the law, at others social obligations. On the more personal side attention by the practitioner to its requirements may well be an influence in determining the judgement of the community, and, not less important, his relations to his colleagues. In a doctor's life it is much for him to know that he enjoys the regard, goodwill, and loyalty of his colleagues. And one way to secure these benefits is to illustrate them by example.

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EUNUCHISM

See ADIPOSITY, Vol. I, p. 202; DWARFISM AND INFANTILISM, ·
Vol. IV, p. 277; PITUITARY GLAND DISEASES; SEX HORMONES;
TESTIS DISEASES; *and* UROGENITAL ORGANS, ABNORMALITIES

EXHAUSTION PSYCHOSES

See PSYCHOSES, TOXIC INFECTIVE

EXHIBITIONISM

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Reference may also be made to the following titles:

PSYCHONEUROSES
SEX BEHAVIOUR, ABNORMALITIES

1.–DEFINITION

455.] As several meanings may be attached to exhibitionism from a clinical standpoint, it will be simplest to begin with the legal definition which is unambiguous.

Exhibitionism is an offence under the Vagrancy Act of 1824, which deems various offenders to be rogues and vagabonds, including 'every person who wilfully, openly, lewdly, and obscenely exposes his person with intent to insult any female'. By 'person' the law means 'penis'.

2.–AETIOLOGY

Exhibitionism is practically confined to men. Legally, of course, it does not exist in women. Nevertheless, it does occur in women, but it is not the genitals but the whole body or some part, such as the breast, which is exposed.

Incidence   In men it occurs as follows: (i) In the young rather than the old; one-

third of Norwood East's cases were under the age of twenty-five. (ii) In
elderly men in whom there is some kind of cerebral degeneration, as
in senile states and arteriosclerotic degeneration. In cerebral syphilitic
disease, especially general paralysis of the insane, it may occur in some-
what younger subjects. It also occurs in chronic alcoholism. Presumably,
with the dysfunction of the higher cortex there is a release of desires
which must have been present previously, though the patient may not
have been aware of them. Indeed such patients have often—outwardly,
at any rate—irreproachable characters. (iii) It occurs in mental defectives,
who constitute a fair proportion of the total cases. (iv) It occurs in
epileptic twilight cases, but, as Havelock Ellis has remarked, the mere
concurrence of exhibitionism with epilepsy is not enough to attribute
the former to the latter. For it to be a true epileptic exhibitionism there
must be no consciousness of the event. It must be entirely involuntary,
like the epileptic incontinence. Such cases, if they exist at all, are
exceedingly rare. (v) It occurs in psychopaths, who are unstable and
generally subject to sudden impulses and moods over which they have
little control. (vi) It occurs in otherwise normal persons in whom the
urge to exhibit themselves is an overwhelming compulsion, of which
they are very much ashamed, and against which they struggle yet are
utterly unable to resist.

3.—PATHOGENESIS

In some cases organic changes are associated with the onset of exhibi-
tionism, but it is difficult to see how such degenerative lesions—indeed,
even if they were irritative lesions—could cause exhibitionistic pheno-
mena. It must be assumed, therefore, that they are merely responsible
for the appearance of an impulse which was previously present but
controlled. There are not any known organic causes of this condition,
and it is necessary to explain it in terms of psychopathology.

The psychopathological explanations are, broadly speaking, along two
lines: (i) anthropomorphic, invoking the reappearance of impulses of an
earlier stage of development; and (ii) psychological, invoking the former
to some extent but offering explanations why the sexual impulse should
remain fixed at what is an infantile form of sexuality. *Psycho-pathology*

In children the desire to exhibit is well marked. This desire is not
confined to the genitals but involves the whole body and the whole of
the child's activities. But the impulse includes the genitals and, as from
parental prohibition the child learns that this is the region which above
all he is forbidden to show, the very attempt at prevention focuses
additional interest and consciousness on this part of the body. This
prohibition is likely to affect boys rather than girls because the girl's
genitals are hidden, and this may be one, though only one, factor in
boys developing exhibitionistic tendencies where girls do not.

A more powerful influence in determining the greater incidence of

exhibitionism in males is probably that females, in spite of an inherent modesty, have a greater right to exhibit themselves, and thus a socially permitted outlet for exhibitionistic tendencies. In some ways there is here an analogy to masochism. Submission, sexually, is natural to women, yet masochism, which might therefore be expected to be commoner in women, is far commoner in men.

Having seen, therefore, how early in life the genitals have become an area of interest, the question remains: What is it that causes the perversion to occur later in life? It cannot be simply a direct reaction to prohibitions against display of the genitals, for such prohibitions are common to practically all children. The explanations put forward are all somewhat involved and naturally highly hypothetical; they may be summarized as follows:

(i) *Hereditary Influence*. Though this has been suggested it is difficult to judge how valid is the evidence, as figures are not given.

(ii) *The Early Occurrence of the Sexual Impulse*. The history often shows that by the age of five many exhibitionists have had strong sexual feelings. They have looked at other children naked, handled them, and allowed themselves to be looked at (possibly showing the beginnings of other perversions, such as sadism); and all these acts have been accompanied by sexual excitement. It is reasonable to assume that such children have difficulty in adapting themselves psychically, for at an early age they have had strong feelings to deal with. They are generally emotional children. The sexual feelings experienced by them have been of a nature which would incur parental disfavour. All this has a tendency to set up psychological conflicts. A realization of having strong desires which are disapproved of tends to give children—or adults, for that matter—an uneasy conscience and a feeling that they are different from others, neither of these attitudes being a psychologically desirable start to life.

'Fixations'   Next, sometimes partly as a result of this early sexual awakening, though not invariably accompanied by overt sexual feeling, psychological 'fixations' may occur; that is to say, the child's interests become fixed on some pleasure or some person, with whom an emotional relationship is started. For the sake of argument, let us assume that a boy has derived sexual pleasure from being watched by his sister while being undressed. This is a forbidden pleasure and, like much forbidden fruit, particularly attractive. Hence there is a strong desire for a repetition of this pleasure which may be looked for in reality or procured by indulging in phantasy. In either event this source of pleasure has become fixed and, even as the child grows up, it is a pleasure which is still sought. Thus, in an otherwise grown-up person there is this 'island' of childish sexual pleasure.

It is along such lines that abnormal sexual impulses develop. In exhibitionism the psychoanalysts hold that there is another specific factor, namely, a fear of castration. This fear may not be conscious. Castration is looked upon by the boy as a punishment for sexual wishes, on the reasoning of an eye for an eye and a tooth for a tooth. The exposure of the

penis is supposed to be in part an attempt to overcome this fear; an act of bravado in which the patient brazens it out, as it were, to prove to his own satisfaction that he can safely expose himself without the feared punishment occurring. Some psychoanalysts would hold that the exposure is an attempt on the part of the patient to reassure himself of the presence of his penis.

These are some, at any rate, of the psychopathological explanations put forward. The question which is not answered is why in some cases there is early sexual development, and how far the conflicts of early childhood and the tendency for them to become fixed may possibly ultimately prove to be associated with glandular secretions. It is not inconceivable that this may be the case, but at present there is not any evidence of it.

In conclusion, it should be mentioned that Havelock Ellis mentioned the occurrence of exhibitionism in 'sexually weak' individuals. To me the meaning of the phrase is not clear: he referred to the fact that such individuals were rarely married, but this is easily explained by the deviation of the aim of the sexual impulse, as a result of which the normal sexual act has no interest for the patient.

4.–CLINICAL ASPECTS

The law makes reference to 'intent to insult a female'. However this may be interpreted legally, it is by no means psychologically sound. The man does not necessarily wish to insult, any more than the woman is invariably insulted. Servant girls, peasant girls, or others referred to as low-class, by which is probably meant that they have not acquired the usual inhibitions, may be pleased to watch the exhibitionist. Indeed, it may be his intention to produce a profound and pleasant effect. A much-quoted case of Garnier's is that of a man who chose a church for the performance of the act. In this case there was apparently no conscious sacrilegious motive, but in such a place the conditions were favourable to the act. The patient gave his reasons for choosing a church as follows: 'Only there has my act its full importance. If I go there it is not to amuse myself; it is more serious than that. I watch the effect produced on the faces of the ladies to whom I show the organ. I wish to see them express a profound joy. I wish, in fact, they would be forced to say to themselves: "How impressive is Nature when seen thus".' Havelock Ellis commented that here was a trace of the feeling which inspired phallus worship. The curious phrasing of the last sentence in the quotation is reminiscent of the type of thought which haunts an obsessive thinker.

The penis may be erect but is often flaccid; that is to say, the excitement may be overtly sexual, or it may be more in the nature of a compulsive act, though differing from a true obsessional compulsion in that it occurs only at intervals. The penis is not exposed to obtain sexual gratification but, as in other obsessional acts, the patient is in a *Manner of exposure*

state of restlessness and tension which is relieved when the compulsive act has been performed. Occasionally other parts of the body, such as the buttocks, are exposed.

In the case of women, as stated previously, when exposure occurs it is the whole body. the breast, or the buttocks but, at least according to the literature, not the genitals.

The act may at once, or later, be followed by masturbation, but rarely by an act of coitus. Often the exhibitionist makes no attempt to approach the object of his exposure. The act is self-sufficient, and after exposing *Place of* himself he is satisfied. The place of exposure is frequently a park, a *exposure* window, or some other place where there are women or girls about but where there are chances of escape. Railway carriages are commonly chosen, and curiously enough a crowded railway carriage may be the chosen spot.

Girls, especially if their legs are bare, are often the recipients of the exhibitionist's attentions. The attractiveness of the woman appears at times to be of little consequence. I know a case of an exhibitionist who frequented a railway, but satisfactory evidence against him could not be secured. He was finally lured to his undoing, greatly to the surprise of the officials, by the railway company's lady detective, a person of very ominous appearance!

5.–COURSE AND PROGNOSIS

On the whole the course tends to be long and the prognosis bad. As the number of exhibitionists diminishes after twenty-five, it appears that there is a certain amount of spontaneous remission. In cases in which the exhibitionism is secondary to disease, as in the elderly, appropriate treatment may put an end to the exhibitionism. In younger people the outlook is more serious, and cases should certainly not be left untreated. The prognosis for treatment will of course vary not only with the fixity, intensity, and duration of the symptoms, but with associated factors, such as the presence of mental defect, epilepsy, and general psychopathy.

6.–TREATMENT

This can be considered under the headings of (i) palliative, (ii) radical, and (iii) punitive.

Palliative   (i) The first task for the practitioner is to win the patient's confidence and let him see that he understands and sympathizes with his difficulties and with his complaint and that, as a practitioner, he is there to help him.

Secondly, if it is at all possible, steps should be taken to see that the patient does not have facilities for going out alone. Havelock Ellis recommended that such patients should be accompanied whenever they went to a place where the impulse was likely to occur. This is obviously

tedious, especially as the complaint is largely chronic, but with the co-operation of the patient it should be possible to restrict the necessity for a companion. Thus, if the patient is able to go to his work along routes where facilities for exposure do not occur, or where he is not subject to the impulse, there is no need for him to be accompanied.

(ii) Direct treatment attempts to reach and eradicate the underlying *Radical* causes of the perversion by such a method as psychoanalysis. It may be *treatment:* said at this juncture that—in my opinion, at any rate—treatment should *direct* aim at finding out the causes of the condition. Methods of suggestion and persuasion may be used in conjunction with such treatment, when they are far more valuable than when used alone. At the same time the patient must be denied facilities for exposing himself.

This is in keeping with the rule that applies to the treatment of neurosis in general, that the satisfaction which the patient is deriving from certain aspects of the neurosis must be prevented. This is not a question of morality, but of therapy. It is by the damming up of this outlet that the patient becomes sufficiently discontented to have a real urge to find other and more desirable means of satisfaction.

As stated earlier, the impulse to exhibit not uncommonly arises at *Indirect* times of stress, and particularly when the patient is depressed. This depression, as likely as not, is endogenous. This does not mean that it is necessarily of the manic-depressive variety but that it is caused by internal psychological difficulties rather than by an outside situation. Some outside situation may be present, but as likely as not the patient is over-reacting to it. Any treatment which can reduce either the frequency or the intensity of these depressive attacks is likely to have a beneficial influence on the exhibitionism.

Here again it is desirable that the patient should be under control, for attempting to reach the causes of the patient's psychological difficulties may be very painful, and there is a tendency for the patient to have an outbreak during the course of treatment. This is undesirable, not only from the patient's point of view but from that of the doctor.

(iii) At present the law punishes exhibitionism by what are on the *Punitive* whole short terms of imprisonment. The uselessness of this procedure is *treatment* shown by the fact that in many instances there is a repetition of the offence immediately on release from prison. In cases in which the impulse is an irresistible obsession in an otherwise normal individual and one who may indeed be acutely ashamed of his complaint, imprisonment is not only futile but brutal.

In some cases imprisonment apparently has a deterrent effect. These are probably cases in which the act is less obsessive and more in the nature of an indulgence; but even then the deterrent effect is doubtful. At Wormwood Scrubs there is a psychotherapist attached to the prison, and a certain amount of treatment is undertaken with apparently some success. Here there is something to be said for imprisonment. Even so, it does not seem right that the victims of what, after all, is an illness should have to suffer the degradation of imprisonment. The

solution should be—as also for other offences of a like nature—some kind of hospital which an offender can be forced to attend for the purpose of receiving the necessary treatment.

There appear to be no satisfactory results of treatment published at present. Dr. W. Hubert, the therapist at Wormwood Scrubs, however, holds not only that treatment is useful but that without it punishment is practically useless.

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EXOMPHALOS

See HERNIA

EXOPHTHALMIC GOITRE

See GOITRE AND OTHER DISEASES OF THE THYROID GLAND, p. 599

EXOPHTHALMOS

See ENOPHTHALMOS AND EXOPHTHALMOS, p. 43

EYE EXAMINATION

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Reference may also be made to the following titles:

BLINDNESS

CONJUNCTIVA, INJURIES
  AND DISEASES

CORNEA, INJURIES AND
  DISEASES

EYELIDS, INJURIES AND
  DISEASES

LACRIMAL APPARATUS
  DISEASES

UVEAL TRACT DISEASES

1.–INSTRUMENTS AND TECHNIQUE OF USING THEM

456.] The satisfactory examination of a patient who complains of eye trouble depends to a very large extent on the ability of the observer to utilize the appropriate instruments. The eye is so small that the details which give the clue to the true condition are only noticed when the illumination is accurately adjusted and the instruments of magnification

are correctly handled. Refinements in this direction are only attained by a lengthy training followed by constant practice, and most practitioners do not get the opportunity for either of these. There is, however, a limited but extremely important field for the general practitioner in the recognition of conditions that are often encountered in general practice and in the diagnosis and treatment of ophthalmic emergencies. It follows from this that the first essential in diagnosis is the possession

of a reliable set of instruments. The expert may be able to manage reasonably well with inadequate means at his disposal, but the inexperienced observer, under similar conditions, may easily miss a most important diagnostic feature.

The majority of conditions for which a patient seeks advice in practice are situated in the anterior part of the eye—the lids, conjunctiva, cornea, or iris. Diseases affecting the deeper parts, such as the retina and optic nerve, are not so common and, as the visual disturbances

FIG. 23.—Focusing lens

are often severe, usually require a specialist's opinion. The tentative first diagnosis in these cases, and the after-treatment, will usually be in the hands of the medical practitioner.

Bearing these considerations in mind, the corneal loupe and condensing lens are of more importance than the ophthalmoscope, and the technique required for the former is probably the more difficult of the two. *Instruments*

The instruments are: (i) a + 13 D focusing lens, preferably with handle (see Fig. 23); (ii) a monocular corneal magnifier or loupe with a magni-

FIG. 24.—Corneal loupe

fication of 10 diameters (see Fig. 24); (iii) the binocular corneal loupe (see Fig. 25), which, though not providing such a high magnification, allows binocular vision, and, being strapped round the forehead, leaves the observer or operator the use of both hands.

The technique required for the use of *Use of* the monocular loupe forms the basis of all accurate observation of *monocular* the affections of the anterior part of the eye, and so must be de- *loupe* scribed in some detail. The patient is seated or stands and the light from a window or artificial source is focused across the patient's nose or from the temporal side on to the eye. The first is the better method, especially when the nose is prominent or the eye deeply set. Observation is then from the temporal side. If the patient's left eye is being examined, the condensing lens is held by the first finger and thumb of the left hand and the little finger of that hand rests on the patient's right cheek to obtain stability. The loupe is held between the first finger and thumb of the right hand, and the right hand rests

on the patient's face, so bringing the loupe near the patient's eye. The observer then bends his head towards the loupe, rests the bridge of his nose on his first finger, and examines through his left eye. The con-
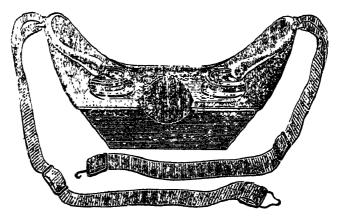
FIG. 25.—Binocular corneal loupe

densing lens and loupe can then be moved backwards or forwards to ensure an accurate light focus and a clear magnified image. The hands holding the condensing lens and loupe are reversed when the right eye is being examined, and the observer uses his right eye. Often the view of the cornea is obscured by the upper lid, which can be gently elevated by the second finger of the hand holding the loupe.

Ophthalmo-scope

HAMBLIN

FIG. 26

Electric ophthalmoscope

For the observation of the lens, vitreous, and fundus, a reliable ophthalmoscope is required (see Fig. 26). With a poor instrument the light reflexes or inefficient focusing may make accurate examination of the details impossible. It is also essential to have a fresh battery and electric bulb in reserve. The ophthalmoscope is designed to afford a clear view of abnormalities in the media and fundus, and so has a battery of lenses of different strengths which can be rotated in front of the sight hole. Opacities in the media will be seen as dark objects against the red background of the choroidal reflex, and for these the higher plus-lenses must be used; +12 for opacities on the back of the cornea; +10 for those in the lens; +8 to 0 for those in the vitreous. In the normal eye, the fundus will be in full focus at 0, but if the eye is myopic, then minus-lenses will have to be rotated in front of the sight hole, and these will vary with the degree of myopia.

In cases of very high myopia it may be difficult to see the fundus details

by this, the direct method, and so the rather more complicated indirect *Technique*
method is needed. A frosted lamp is placed behind the patient and *for cases of*
slightly above the shoulder on the side being examined. The observer *high myopia*
has a concave mirror with a +2 dioptric lens fixed in the sight hole. He
holds this in his right hand between the first finger and thumb, with the
little finger of this hand fully extended. The light is then thrown into the
eye and condensed by a ÷13 lens held by the other hand a few centi-
metres in front of the eye. If the patient's right eye is being examined
he is instructed to look at the tip of the little finger: if the left eye, at the
observer's left ear, when the corresponding disc becomes quite clear.

By moving the condensing lens slightly from side to side, other details
round the disc are brought into view. The macula can be investigated
when the patient looks straight at the light, and the periphery when he
looks to right and left or up and down.

2.–ROUTINE EXAMINATION

457.] A routine method of examination should be used for any patient
who complains of his eyes. An irritable eye may depend on an inturned
lash, a foreign body under the lid, a corneal ulcer, commencing con-
junctivitis, or iritis, and so it is necessary, and in fact more rapid in the
end, to work out a plan which will prevent some unexpected factor from
being missed.

The history is first taken, and the visual acuity with or without glasses
noted. The eye is then examined in the order: lids, conjunctiva, lacrimal
apparatus, cornea, iris, and pupil reactions—these with the loupe: and
then lens, vitreous, and fundus—these with the ophthalmoscope, starting
with a + 12 D lens in the sight hole and working down to 0.

Certain features of importance in this routine examination of the
different parts as they apply to a patient suffering from lacrimation,
irritation, pain, or inflammation will now be dealt with.

(1)—Lids
These should be examined for inverted eye-lashes, which may be ex- *Eye-lashes*
tremely fine and which, though more often associated with chronic
blepharitis or injuries to the lid margin, are found in quite normal lids.
A lash may get into a Meibomian gland or even into the punctum
lacrimale and cause irritation of the cornea or conjunctiva with each
movement of the lids.

(2)—Conjunctiva
This should be inspected for evidence of foreign bodies or conjunc- *Foreign*
tivitis. The former are most frequently found under the upper lid and so *bodies*
the technique of everting this should be acquired. The procedure can
be easily carried out over a glass rod—the main point being that the
patient *must* be looking down during the manœuvre. Chalky deposits

are often found in the mucous glands of the conjunctiva, especially of the lower fornix. When these project through the surface layers they cause irritation.

Conjunc-
tivitis
Conjunctival injection may be present with or without any discharge. It may be most marked in the fornices or on the bulbar conjunctiva, and the differentiation between early conjunctivitis and iritis is not always easy. In conjunctivitis the redness is usually more marked in the fornices and the conjunctiva may look swollen or granular. There is usually some watery or muco-purulent discharge. The cornea is bright, and the pupil active.

(3)—Lacrimal Apparatus

Interference with the drainage system or excessive production of tears produces lacrimation and epiphora. Examination of a case which shows these symptoms includes therefore search for a possible source of irritation in lids, conjunctiva, and cornea, and then examination of the nasolacrimal duct.

Dilatation of
punctum
lacrimale
The punctum lacrimale can usually be seen with the loupe. In old people it often closes up or becomes everted from the globe, and a minor operation is required for dilatation. Slitting the orifice for a millimetre or two is very efficacious in some of these cases.

Pressure on the lacrimal sac will determine if there is any regurgitation of muco-pus into the conjunctival sac. Regurgitation confirms a block in the lower nasal end. If there is no regurgitation, a few drops of fluorescein or methylene blue should be instilled into the conjunctival sac and the patient asked to blow his nose. If the dye passes through, the passage is clear. A more satisfactory method is to dilate the punctum lacrimale and syringe some fluid into the sac. If there is a blockage, the fluid will return through the upper punctum; if the passage is clear, the patient will feel the fluid pass into the nasopharynx.

(4)—Cornea

Use of
fluorescein
An examination should be made with the loupe for any local or general loss of lustre in the corneal epithelium, and the procedure should be repeated after staining with fluorescein. Any abrasion of the surface will take up the green stain and become at once quite obvious. Many small traumatic abrasions, the minute staining spots of superficial punctate keratitis and ulcers of the dendritic type are quite unrecognizable with the loupe alone. It should be a routine to stain every red or irritable eye with fluorescein, which can be kept in lamellar form or as a 2 per cent alkaline solution. The lamella or solution is put into the conjunctival sac and left for a minute and the excess is then washed out with saline or boric acid solution so that all the stain is removed except that which has become fixed in the damaged tissue of the cornea.

In burns of the eye caused by chemicals, such as acids, alkalis, or lime, it is important to find out the extent of the damage to the cornea and conjunctiva. Fluorescein will stain the cornea green and the conjunctiva

yellow, and treatment depends very much on the extent of the damage
to these tissues.

In every inflamed eye it is necessary to examine the endothelium lining *Examination*
the anterior chamber for evidence of cellular deposits (keratic precipi- *for keratic*
tates or K.P.). These clumps of leucocytes and fibrin originate in the *precipitates*
ciliary body and pass into the anterior chamber. They are often pig-
mented and are more often seen in the lower half of the eye (see Fig. 27).
If fine and non-pigmented, K.P. is very easily missed; but as the condi-
tion indicates an inflammation of the very important ciliary body its
detection is essential. Sympathetic ophthalmia is a cyclitis and choroid-
itis affecting one eye following upon a perforating injury to the other

(a)　　　　　　　　　　　　　　　　(b)
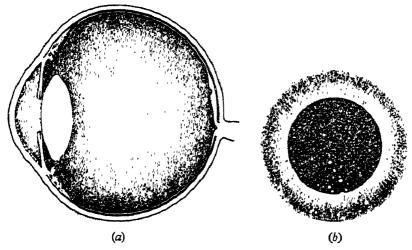
FIG. 27.—Keratic precipitates. (a) Section of eye showing deposits
on endothelium lining anterior chamber; (b) the same seen with slit-lamp

eye. The first evidence of this very serious condition is fine K.P. and
oedema of the endothelium.

With the loupe a fairly adequate view of conditions in the different *Corneal*
layers of the cornea can be obtained, but as a refinement there is the *binocular*
corneal binocular microscope with slit-lamp illumination (see Fig. 28). *microscope*
By this method of illumination a beam of light of varying width passes
through the cornea. This 'optical section' of the cornea is examined
through a binocular microscope and the magnification is sufficient for
the identification of the individual cells of the epithelium and endo-
thelium, of blood corpuscles in newly formed vessels, and of the earliest
signs of inflammation. For this reason, examination by the slip-lamp
has been called the microscopy of the living eye. By this method many
hitherto obscure corneal conditions have been more clearly defined,
and it is particularly valuable in the early recognition of changes in
the cellular contents of the aqueous and in the endothelium lining the
anterior chamber.

In cases of perforating injury of the globe, when sympathetic ophthalmia

is to be feared, a dark examination of the uninjured eye is made, and the evidence from this source may be the main factor in the surgeon's decision to remove the injured eye.

Estimation of depth is very much simplified. Superficial, interstitial,
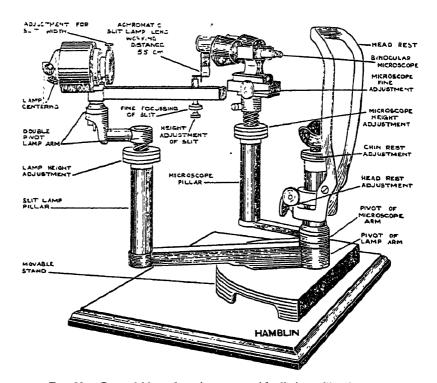
FIG. 28.—Corneal binocular microscope with slit-lamp illumination

and deep new vessels can be differentiated. The depth of an embedded foreign body may be estimated, and K.P. unappreciated by the loupe can be clearly demonstrated.

(5)—Iris

The iris pattern in the two eyes should be compared. Oedema and congestion give a muddy appearance. The pupil reactions should be noted and an examination made for adhesions to the lens.

Iritis, as distinct from conjunctivitis, shows a circumcorneal or ciliary congestion. The fornices are normal and there is not any discharge. There may be considerable pain, and the eye may be tender on pressure. The pupil is usually smaller than that on the other side, and the reactions are more sluggish.

Differential diagnosis It is important to differentiate between acute iritis and subacute or acute glaucoma. The main points in the diagnosis of these conditions and in their differentiation from conjunctivitis are set out in the following table:

CONJUNCTIVITIS	ACUTE IRITIS OR IRIDO-CYCLITIS	ACUTE GLAUCOMA
Congestion chiefly in fornices	Ciliary congestion	Ciliary congestion
Discharge	No discharge	No discharge
Cornea bright	Cornea bright	Cornea hazy. Marked loss of surface lustre
Pupil normal	Pupil smaller than that of opposite eye. May react sluggishly or be bound down by adhesions K.P. may be present	Pupil larger than that of opposite side; often oval and sluggish or even inactive
Tension normal	Tension normal	Tension raised
Atropine unnecessary	Atropine imperative	Atropine contraindicated

It will be seen that the size of the pupil, the condition of the cornea, and the tension are the points to note in differentiating between acute iritis and acute glaucoma; and as wrong treatment may mean loss of the eye, careful examination is needed. The tension can be estimated *Estimation* fairly accurately with the fingers. The first fingers of each hand are rested *of tension* gently on the upper lid, with the patient looking down. Pressure with these alternately will cause some dimpling of the sclera in a normal eye. In glaucoma the eye is hard and no dimpling is felt. A more accurate method is by means of the Schiötz tonometer, which records the tension when applied to the cornea with the patient in the recumbent position.

(6)—Lens

The two most valuable methods for the examination of the lens are the slit-lamp and the ophthalmoscope with a +10 in the sight hole.

The slit-lamp has revolutionized our knowledge of congenital and *Slit-lamp* acquired lens opacities. It has shown that the lens is made up of different nuclear layers—laid down at different periods in the growth of the organism. By examination of the optical section of the lens the age period of opacities can be very accurately gauged, and so our knowledge of the natural history of lens opacities has been greatly advanced.

(7)—Vitreous

Only the anterior layers of the vitreous can be investigated easily with the slit-lamp and corneal microscope, but with the ophthalmoscope and varying strengths of plus lenses from +8 to 0 in the sight hole, it can be explored for opacities of different types—congenital, inflammatory, *Opacities* or haemorrhagic. These are seen as dark spots of different shapes against the red fundus-reflex, but, unlike those in the lens, they all float to a certain extent with movements of the patient's eye.

(8)—Fundus

Mydriatic

For a satisfactory examination of the fundus, a mydriatic is usually needed. It is quite safe to instil two drops of 2 per cent homatropine if eserine 0.5 per cent is used as a neutralizing agent afterwards. To find the disc it is necessary to look slightly obliquely inwards with the patient gazing straight in front of him. The four sets of vessels should then be followed from the disc to the periphery, and changes noted in their appearance, calibre, and tortuosity. The periphery is searched next, and then, returning to the disc, the practitioner measures two disc diameters to the temporal side and examines the macula.

(9)—Disc

Normal variations

If the opportunity is taken to examine many healthy fundi, it will be seen how much variation there can be in the disc within normal limits. The normal disc-edge can be seen clearly in its whole circumference, but it is usually more defined on its temporal half because there are fewer nerve-fibres passing across this side. For the same reason, the nasal half of the disc is less distinct. There is usually a depression occupying the centre and temporal part of the disc—the physiological cup—and emerging from the nasal side of this depression are the retinal vessels (see Fig. 29).

FIG. 29.—Normal optic disc. A and B indicate vessels which must be examined in cases of papilloedema. (This and the following illustrations from the Author's *Ophthalmology in General Practice*)

The retinal vessels pass over the edge of the disc without any kinking, and if at this point a vessel is focused with the highest plus-lens in the sight hole, then any other vessel or branch within a disc diameter of the edge running in the same direction will be in focus with the same plus-lens, and both will be out of focus with a higher plus-lens. This observation is important because a higher reading for the vessel on the disc-edge would indicate some swelling of the disc; and if it were supplemented by blurring of the disc margin, increased size and tortuosity of the vessels, filling up of the physiological cup, and perhaps some scattered haemorrhages, a diagnosis of papilloedema might be made. In

Atrophy

atrophy the disc is pale. In primary atrophy the margin is clear, the physiological cup obvious, and the vessels normal. In secondary atrophy the disc margin is blurred, the physiological cup is filled in, and the

Chronic glaucoma

vessels are narrow. Chronic glaucoma produces a very pale disc with the added feature of deep cupping or excavation. In this event the vessels

are kinked as they cross the rim of the cup, and there is a difference of level, which can be estimated with the ophthalmoscope, between this point and the bottom of the cup.

(10)—Retinal Vessels

These vessels being magnified fifteen diameters can be seen very clearly with the ophthalmoscope, and recognition of changes in them may be

(a)   (b)

(c)
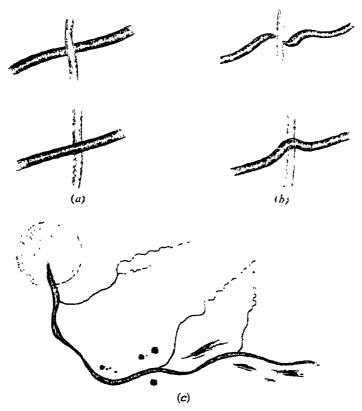
FIG. 30.—Retinal vessels. (a) Normal; (b) pathological; (c) irregular lumen in arteriosclerosis

of great value in the diagnosis and prognosis of high blood-pressure and renal disease. What is actually seen on looking at a retinal artery or vein is the column of blood within it, the vessel wall being transparent. The coats of the vessel only show their presence by a light reflex or bright line which extends along the centre of the blood column (see Fig. 30).
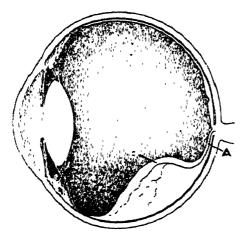
In arteriosclerosis there is first a loss of translucency in the arterial *Arterio-* wall; later the light streak becomes wider and more marked, and the *sclerosis* artery looks more like a burnished copper wire. More easily noted are the changes where an artery and vein cross one another. Normally the two columns of blood meet and cross without any kinking or deflection,

but where the arterial wall is hard, the vein will be compressed or deflected. Other signs of sclerosis are increased tortuosity of the vessels and general narrowing or local irregularity in the width of the lumen. White lines may be seen along the side of the column of blood. These are evidence of thickening in the coats, whereby the vessel wall, normally transparent, becomes partly visible with the ophthalmoscope. Retinal haemorrhages may occur or white spots of exudation either along the vessels or at the macula.

(11)—Macula

No details are visible at the macula in a normal eye. Any raised or yellowish patches or signs of pigmentation indicate some pathological condition which needs investigation.

(12)—Fundus Periphery

Any gross change will make some alteration in the quality of the fundus reflex. Thus, if there is some retinal or choroidal disturbance below, the reflex will have a yellowish or greenish appearance as compared with the normal red colour in the rest of the periphery.

Scars

Scars of old choroido-retinitis are often seen in the periphery or scattered clumps of pigment from

FIG. 31.—Retinal detachment. The section shows (A) vessels at the disc and (B) on the detached retina

Retinal detachment

other causes. Occasionally when examining the vitreous it will be noted that retinal vessels can be focused with a high plus-lens in one direction, whereas near the disc they are only seen with a 0 or minus-lens in the sight hole. It is then obvious that these vessels must be lying well anterior to their normal position. As they are within the retina, the retina itself must be bulging forwards and a diagnosis of retinal detachment can be made (see Fig. 31). This may be missed unless the routine method is adopted, as the retina itself is transparent.

(13)—Perimetry

Object of perimetry

The object of perimetry is to detect and locate defects in the visual apparatus. In the retina, in a cross section of the optic nerve or tracts, and in the occipital cortex there are corresponding points, and so a defect in the visual field will give a clue to the position and perhaps to the nature of the pathological condition in the nerve pathway or the higher centres.

The perimeter is mainly used for the examination of the peripheral

field. When the central field up to the 30° circle is being investigated, it is advisable to use a screen and work at a greater distance—about two metres—so that the defect is increased in size and can be more accurately mapped out. The following methods are employed:

The Confrontation Method

This is a rough method which can be carried out with the hands and *Method without apparatus* needs no apparatus. If the patient and surgeon face one another and the patient's left eye is being examined, he will fix the surgeon's right eye with his left eye—both patient and surgeon having the other eye closed. The surgeon holds out his hand in the extreme periphery of the visual field and slightly moves his fingers. If the surgeon can detect this movement, the patient, if his visual field is full, should be able to do so too. A marked contraction or sector loss is easily demonstrated by this method.

The Perimeter Method

The perimeter may be self-registering or non-self-registering, but the *Types of perimeter* former is very much to be preferred. The illumination is constant and for this reason charts taken at intervals have a real comparative value.

The patient is seated with his chin on the rest and the eye not under *Technique* examination securely occluded. If visual acuity is good, a small $\frac{1}{2}°$ white object is used on the perimeter arc, and the patient taps on the table as soon as he notices that it is moving towards the fixation-spot. It is important to watch the patient carefully to see that his eye does not wander from the central fixation-spot during the examination. A reading is made for every 10 or 20 degrees and the machine records the result on the chart. There are certain important points in this investigation that are often neglected. The natural obstructions to a full field must be *Elimination of obstructions* eliminated as far as possible, otherwise the charts may be of very little value. Thus, when the upper field is being charted the upper lid must be elevated by the surgeon, the eyebrow lifted, and the patient's chin tilted upward slightly. In charting the nasal field, the prominence of the nose must be overcome as far as possible, the patient's head being turned towards the opposite eye. In charting the lower field, the head must be tilted downwards to eliminate the prominence of the malar bone. The temporal field having no bony obstruction, such precautions are not needed. With each movement of the head, the eye must of course still fix the central spot of the perimetric arc.

If these precautions are not taken, a patient with a deeply sunken eye may show a markedly contracted field, simulating that found in glaucoma. In cases with poor vision, a correspondingly large object must be used on the arc, and if the patient is unable to distinguish even this, his field can be charted very roughly with light projection, as is done in cases of mature cataract when it is important to know that the retina is functioning in all parts.

The Screen Test

Technique

A Bjerrum screen consists of a large dark cloth screen with a central fixation-spot. The screen is marked out with concentric circles and radiating lines in black cotton—invisible to the patient. A test object on a long handle is moved across the screen, and any blind spot or area of lowered visual acuity can be mapped out with black pins. The area is then transferred to a chart for record.

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EYE, HEREDITARY DISEASES

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Reference may also be made to the following titles:

1.–MODE OF INHERITANCE OF EYE DEFECTS

458.] Ophthalmology was singled out by Karl Pearson as a branch of medical science in which the importance of heredity studies had been fully appreciated. In drawing attention to recent published work, he

Anomalous mode of inheritance of eye defects   especially praised the achievements of Nettleship. Another factor which closely links ophthalmology with the study of heredity is the existence of two distinct modes of transmission for certain hereditary ocular defects. Punnett pointed out that this anomaly has no close parallel in animal genetics; he referred particularly to those defects which may behave either as simple Mendelian dominants, or as sex-linked recessives, without any clinical differentiation between the types from these two sources.

Significance of Mendelism   The importance of Mendel's work is firmly established, but recent additions to knowledge make it impossible to accept Mendelian laws as a complete explanation of the facts of heredity. Penrose pointed out that the ultimate criterion of the application of the Mendelian interpretation to the data supplied by family histories is numerical, and that pedigree studies are not conclusive of this kind of inheritance unless the simple Mendelian ratios are found on analysis of the affected families. Punnett believed that a proper understanding of the physiological basis of hereditary defects is more important than the application of mathematics to insufficiently established data. Julia Bell pointed out how easy it is to draw fallacious conclusions from pedigrees which, though at first sight anomalous, can by more careful investigation be explained on ordinary lines. Ida Mann and others referred to the multiple hereditary defects which often arise spontaneously in experimental animals, especially when there has been much inbreeding.

van Duyse's classification   Concerning the mode of inheritance of ocular defects, van Duyse supplied the following classification:

A. Transmitted as Mendelian *dominants*: essential night-blindness, congenital and senile cataract, single ectopia lentis, familial corneal degeneration, blue sclerotics, total and partial congenital ophthalmoplegia, typical and atypical colobomas.

B. Transmitted as Mendelian *recessives*: total albinism, retinitis pigmentosa, hydrophthalmia, amaurotic family idiocy.

C. Transmitted as recessive *sex-linked* characters: Daltonism (i.e. colour-blindness), Leber's hereditary optic atrophy, and certain forms of nystagmus.

Other rare eye conditions   Several rare but interesting conditions might be added to this list, e.g. distichiasis, aniridia, and possibly opaque nerve fibres to group A; the Laurence-Moon-Biedl syndrome (i.e. obesity, hypogenitalism, mental retardation, polydactyly, and retinal pigmentation) to group B; megalocornea to group C. Waardenburg has pointed out that the following conditions known to be transmitted by sex-linked inheritance can also occur as dominants: nystagmus, zonular cataract, macular degeneration, night-blindness, retinitis pigmentosa, and myopia. Julia Bell's work on Japanese material indicates that Leber's hereditary optic atrophy may also be regarded as having the same double means of transmission. It is proposed to consider in more detail some of the above-mentioned ocular conditions from the clinical point of view.

2.—INHERITED EYE DEFECTS

(1)—Retinitis Pigmentosa

459.] This is a slowly progressive disease, whose earliest symptom is inability to see well in a dim light. It has long been known to occur in families (see Figs. 32 and 33), and there are numerous instances of carefully worked-out pedigrees, e.g. by Nettleship and Usher. Usually the
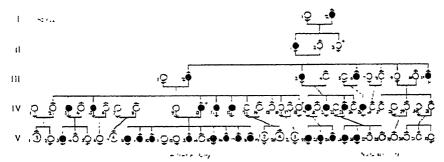
Fig. 32.—Twenty-nine cases of retinitis pigmentosa in five generations: night-blindness in all cases appears to have been present in early childhood or infancy; at about the age of forty those affected became practically blind. (This and the following pedigrees are from *Eugenics Laboratory Memoirs*)

degeneration appears to act through the medium of the choroidal capillaries, with resulting impairment of nutrition in the outer retinal layers. In the earlier stages, the mid-periphery is the region chiefly affected, but in time the whole of the retina becomes involved.

A history of inability to see in a dim light, especially after inquiry has elicited the presence of a similar failing in other members of the family, strongly suggests this disease, and, in most cases, the diagnosis is easy, although difficulty sometimes arises from the fact that the onset of night-blindness may precede visible changes in the fundus. These consist characteristically of curiously arranged areas of abnormal pigmentation occurring chiefly in the mid-periphery. The areas of pigmentation are very often disposed in a shape
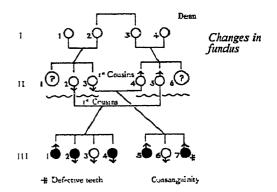
Fig. 33.—Two sisters married two brothers, their first cousins; five cases of retinitis pigmentosa occurred with two normal persons in the resulting sibships

that is reminiscent of bone corpuscles, or of neuroglia as displayed by Golgi's method of staining. Sooner or later the pigmentation spreads to the extreme periphery, and makes its appearance also in the central portion of the fundus. There is also well-marked progressive shrinkage of the retinal vessels, combined with a yellowish

wavy appearance of the optic disc. In the later stages, a complicated cataract is slowly formed, beginning, as complicated cataracts always begin, with a small zone of opacification in the hindmost layers of the posterior cortex, and exhibiting polychromatic lustre in the zone of specular reflection on examination with the slit-lamp.

Prognosis   The course of the disease may be exceedingly slow, and central vision often remains good for many years after the appearance of gross, widespread, pigmentary degeneration. The ultimate prognosis is bad, and probably none of the numerous methods of treatment that have been recommended are of any value.

Associated defects   Retinitis pigmentosa is one of several hereditary diseases which may be associated with defects in other parts of the body or, as Nettleship pointed out, the defective transmission may appear in different guises in the various generations or individuals. For instance, retinitis pigmentosa may alternate with deaf-mutism in the same sibship. This phenomenon is known as dissimilar or equivalent inheritance.

(2)—Essential Night-Blindness

460.] This differs from retinitis pigmentosa in four important respects: it is non-progressive, is present from birth onwards, is unaccompanied
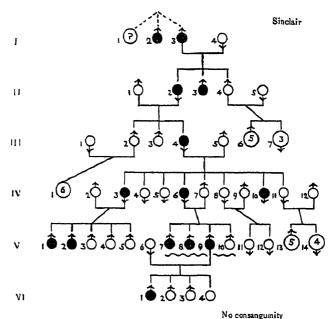
Fig. 34.—Fourteen cases of congenital stationary night-blindness in six generations

Common ancestor   by fundus changes, and is regional. This interesting condition has been the subject of an enormous amount of pedigree research, and has now been traced back to Jean Nougaret, an inhabitant of Vendémian in the 17th century. Up to 1907 when Nettleship was writing on this disease, more than 2,000 members of the pedigree had been traced: 72 males

and 62 females out of this number were known to be, or to have been, night-blind. The investigation was started more than a century ago when a young conscript, a member of the affected stock, claimed exemption from military service on the ground that he could not see at night. It is not surprising that he was supposed to be a malingerer, as he could see quite well by candle-light. Having done compulsory military service
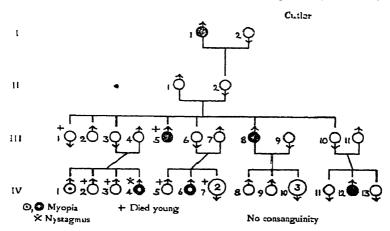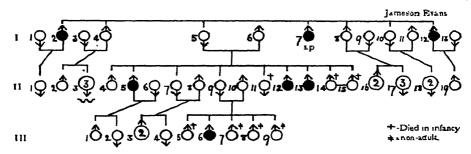
FIG. 35.—Sex-linked recessive night-blindness

for seven years, he was re-examined more thoroughly. When it was found that he was speaking the truth, research into his near relations began. In recent years a similar night-blindness has been investigated by Truc and Opin in Néoules, a small village near Toulon, comparatively isolated until lately; 42 out of 142 reputed sufferers were traced, but it was not possible to find a common ancestor, as was done in the Vendémian pedigree. The investigators suggested that Nougaret was possibly a native of Néoules, and that these cases were among his descendants. Figs. 34 and 35 show characteristic pedigrees.

(3)—Leber's Hereditary Optic Atrophy

461.] This condition is transmitted to males, and much less commonly

FIG. 36.—Leber's hereditary optic atrophy in seven males of three generations

to females, by females who are usually unaffected (see Fig. 36). Lagrange found that the coagulation rate of the blood was retarded in a boy of

Changes in the eye

eighteen suffering from this disease; this is of interest as haemophilia has the same sex-linked method of transmission. Both eyes are involved sooner or later, but the original onset may be in one eye only. The failure of sight is fairly rapid for some days, but blindness is never complete, and remissions may occur, although the ultimate result is invariably a serious diminution in sight. There may be some blurring of the edges of the disc during the acute stage, but there is never any gross swelling. When the condition has fully developed, the disc presents some degree of secondary optic atrophy.

(4)—Cataract

462.] Saunders (1811) pointed out that cataract may attack successively children of the same parents, and he gave instances of this phenomenon. Some forms of cataract are definitely hereditary, especially the characteristic form in which the onset is during childhood, and the opacities are varied in shape and in colour. This type of cataract is very slowly progressive, and instances of it have been traced through at least four generations. Rowan and Wilson published a pedigree showing hereditary cataract in four generations. Morphologically it resembled senile cataract, but its onset was between the ages of thirteen and eighteen. According to Koby, anterior polar cataract can be transmitted as a

Appearance of lens

Mendelian dominant. The following description applies to the lens (the fellow lens having been already needled) in a man twenty-three years old in the second generation of a family among whom I examined representatives of three generations suffering from slowly progressive hereditary cataract: 'The anterior Y is prominently mapped out in blue. There are numerous blue, green and violet dots, chiefly in the adult nucleus and in the superficial layers of the foetal nucleus. These dots are somewhat larger than those that are customary in ordinary lamellar cataract. The deeper layers of the foetal nucleus, as well as the whole of the central dark interval, are full of greyish-brown strands resembling a broken network. A large number of crystals are visible in the cortex and in the adult nucleus.'

'Anticipation'

It is true that in many families there is a demonstrable hereditary predisposition to ordinary senile cataract, and many pedigrees have been constructed purporting to show that this is one of the conditions in which 'anticipation' occurs. 'Anticipation' used in this context means that the tendency is for the condition in question to make its appearance at an earlier age in successive generations. Many modern authorities, however, regard 'anticipation' as a statistical fallacy.

(5)—Blue Sclerotics

463.] Blue sclerotics is the name given to a form of hereditary disease in which the sclerotic coat fails to attain its normal thickness, so that the underlying pigmented layers impart a bluish appearance to the

Associated defects

white of the eye. In many cases of this disease, defects in other parts of the body are associated, especially in the bones, which are abnormally

fragile. Sometimes otosclerosis develops, with resulting deafness (see Fig. 37).

(6)—Distichiasis

464.] Distichiasis means a double row of lashes. In most cases, the hairs *Definition* and their follicles take the place of the Meibomian glands, so that the accessory row is seen sprouting from what would have been the orifices of the Meibomian ducts on the lid margins. All four lids are usually involved, but symptoms tend to be absent in the first few years of life owing to the fine, downy texture of the accessory cilia. Occasion-
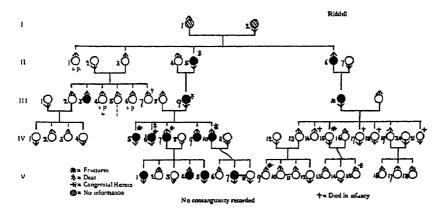
FIG. 37.—Blue sclerotics in six males and eight females of four generations

ally there is more than one row of extra lashes. Erdmann recorded distichiasis in a girl whose mother and grandmother were both affected. The treatment of these cases may be exceedingly difficult. Epilation is *Treatment* not applicable, because the removed lashes simply grow again. When these are not very numerous, the most convenient method is electrolysis of each follicle. In cases with numerous lashes, however, this method of treatment is tedious and difficult, so that some operation has to be devised. Von Szily performed an intermarginal section, and detached the posterior lash-bearing area by an incision parallel to the lid-margin. (See also EYELIDS, INJURIES AND DISEASES, p. 240.)

(7)—Cerebro-Retinal Degenerations

465.] Amaurotic family idiocy or Tay-Sachs' disease and Batten's disease are considered under the title CEREBRO-RETINAL SYNDROMES OF THE HEREDO-DEGENERATIVE TYPE, Vol. III, p. 30.

(8)—Colour-Blindness

466.] Colour-blindness is transmitted by the sex-linked mode of inherit-ance, and is about ten times as common in males as in females (see Fig. 38). It may be partial or complete. The complete form is compara- *Associated* tively rare, and is always associated with nystagmus and central scotoma. *defects* All objects appear as some shade of grey. In the partial form, the com-

on most subdivision is the red-green variety. This is the well-known form of colour-blindness, the possible existence of which must be carefully excluded in examination of candidates for occupations such as engine-driving or ship-navigation, in which it is essential that a person should
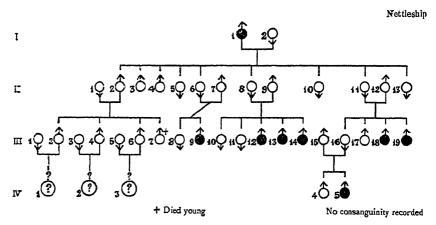
FIG. 38.—Colour-blindness in eight males

distinguish between red and green signals. Riddell (1937) published a pedigree showing the occurrence of haemophilia and colour-blindness in the same family. (See also article COLOUR VISION, Vol. III, p. 334.)

(9)—Albinism

467.] Albinism, like other disabilities transmitted as Mendelian recess-ives, is much more likely in the offspring of consanguineous marriages.

Associated defects

The complete form is always associated with nystagmus, and errors of refraction are frequently associated. Vision even with the aid of correct-ing lenses never comes up to fully normal standards. (See also ALBINISM, Vol. I, p. 271.)
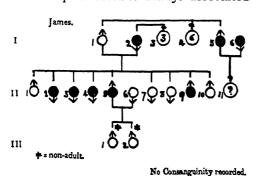
FIG. 39.—Glaucoma, five cases in a sibship of ten

(10)—Glaucoma

468.] Glaucoma has a tend-ency to run in families (see Fig. 39), and this is one of the diseases in which pedigrees have often been constructed to show 'anticipation'. This tendency was noted by von Graefe as long ago as 1869. (See also GLAUCOMA, p. 108.)

(11)—Glioma

469.] Griffith published records of two families in which the mothers, both of whom had had an eye removed for glioma, transmitted the

disease to several of their children (see Fig. 40). He believed that these hereditary cases are more likely to show a bilateral tendency. Berrisford recorded the case of a man whose eye was removed for glioma. His
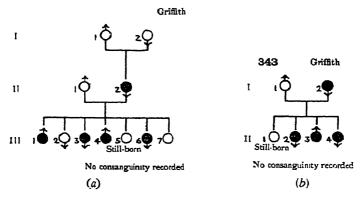
FIG. 40.—(*a*) Four cases of hereditary glioma of retina in sibship of six born alive.
(*b*) Three cases in sibship of three born alive

daughter was free from the disease, but her four children all developed glioma, three of them bilaterally.

(12)—Nystagmus
470.] The classification of nystagmus is a complicated and controversial subject which it is impossible to treat adequately here. As a result of his extensive studies of family trees, Hemmes divided hereditary nystagmus into two groups, of which the first affects males and females indifferently, whereas in the second the defect is transmitted by females but only affects males. (See also NYSTAGMUS.)

(13)—Other Conditions
471.] Familial tendencies can often be traced in such various conditions as the jaw-winking phenomenon, microphthalmia, ptosis, word-blindness, defective light sense, and others. Davenport published a pedigree showing the occurrence of choroidal sarcoma in the families of three successive generations.

3.—INHERITANCE OF ERRORS OF REFRACTION

472.] The influence of heredity on the refraction of the eye is a subject about which a great deal of research remains to be done, but there is no doubt that myopia is in a large number of cases inherited. This is what *Myopia* would be expected, considering that the size of the eyeball is an important factor in determining the refraction, and the size of the eyeball is, of course, likely to be closely affected by heredity.

There is no general agreement about the extent to which squint is a *Squint* hereditary disease, but evidence appears to be accumulating that this disability is often familial, not only as a result of direct inheritance of

the squint as such, but by reason of the kind of inherited nervous dis-
position which would, in fact, make the development of a squint more
likely. This indirect influence of one factor in making the inheritance
of any particular condition more likely is becoming increasingly recog-
nized. It is possible, for example, that in some families in which several
members are affected by lamellar cataract, the inheritance of the defect
is brought about through the medium of some passing derangement of
metabolism, as a result of which the nutrition of the lens is temporarily
impaired. so that a zone of opacity develops.

Lamellar
cataract

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EYELIDS, INJURIES AND DISEASES

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1.–CONGENITAL ANOMALIES

473.] Epicanthus is a semilunar fold of skin which covers the internal *Epicanthus* canthus (see Fig. 41). In the Mongolian race a moderate degree of epicanthus is the rule, and produces a characteristic appearance of the palpebral fissure in these people. It may be due to a lack of development of the bone of the base of the nose. It is undesirable to treat epicanthus by operation until ample time has been allowed to elapse for further growth of the nasal bones which may alleviate the condition. Operation

consists in the excision of a lozenge-shaped area of skin from the dorsum of the nose. More elaborate plastic operations have also been suggested.

Coloboma   Coloboma of the upper lid is a fissure, having the shape of a triangle with its base at the border of the lid. A plastic operation to cure the condition should be carried out at an early period by a surgeon accustomed to carrying out operations on the eyelids.

Ptosis   Ptosis may affect either one or both eyes. The upper lid cannot be raised completely so that the palpebral fissure is not fully opened and the pupil is partly covered by the upper lid. To remedy this the patient contracts the frontal muscles and throws his head backwards. Operation for congenital ptosis should be carried out before the age of ten. If the superior rectus is strong and healthy the tarsal plate may be attached to it, so that the upper lid is raised when the eyes are directed upwards (Motais's operation modified); or the tarsus may be excised (Feigenbaum). A number of other operations have been devised for ptosis, most of which are unsatisfactory.
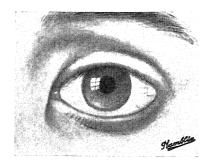
Naevus   Naevus or diffuse angioma of the eyelid of limited extent can be dealt with by radium or by electrolysis by a medical man skilled in radio-electrical treatment. An angiomatous tumour which extends into the orbit, or which commencing in the orbit causes the eye to become thrust forward (proptosis), presents great surgical difficulties.

FIG. 41.—Epicanthus

Distichiasis   Distichiasis is a congenital condition in which there are two rows of lashes, an anterior row which is directed forwards, and a posterior row which is directed backwards and rubs the cornea (see p. 235). The condition often affects all four eyelids. Treatment is operative; a mucous membrane graft is placed behind the posterior row, so that the lashes can no longer irritate the cornea. If desired for cosmetic purposes, the anterior row of lashes may be excised together with the horizontal strip of skin which bears them.

Blepharophimosis   Blepharophimosis is a condition in which the palpebral fissure is narrow. This may be congenital, or may be the result of cicatricial changes in the conjunctiva. When the condition is well-marked, or when treatment of a diseased conjunctiva is prevented by the difficulty in everting the upper lid, the operation of canthoplasty should be performed.

2.—INJURIES

Ecchymosis   474.] Ecchymosis may be the result of the migration of extravasated blood in a fracture of the base of the skull. Direct violence, even when slight in degree, may cause marked swelling of the lids with bluish-black

discoloration from effusion of blood. This is of little importance if the eye is uninjured. It is necessary, in such a case to get an adequate view of the globe by raising the upper lid with a retractor or any blunt hook, and to note that no damage has been done by observing that the pupil is round and reacts to light.

Emphysema implies the presence beneath the skin of air which has *Emphysema* escaped from one of the accessory nasal sinuses as the result of a fracture of bone by violence which may have been slight. The condition is of little importance when unaccompanied by other pathological signs.

Wounds of the skin should always be cleaned up and sutured as soon *Wounds* as seen, taking care that accurate apposition of the edges is effected, otherwise deformity will result. Fine black ophthalmic silkworm-gut sutures, used with a number-4 curved ophthalmic needle and needle-holder, if available, should be employed.

3.—INFLAMMATION

475.] Hyperaemia of the lid margins may be significant of an uncorrected *Hyperaemia* or inefficiently corrected error of refraction. The treatment is to provide the necessary glasses. In other cases the hyperaemia may be due to focal sepsis situated in the tonsils, or in the mouth where there may be a devitalized tooth with an abscess at its root. These conditions may be minimized, but not cured, by the application of ammoniated mercury ointment 2 per cent.

Blepharitis is due to a bacterial infection of the skin margins of the lids (see Fig. 42). It is commonly seen in young children during an

Blepharitis

FIG. 42.—Blepharitis

attack of measles, when it should be carefully treated by the application of ammoniated mercury ointment 2 per cent. In the same subjects it may be due to the presence of enlarged and septic tonsils; the throat should always be examined in cases of blepharitis. The margins of the lids are red and inflamed, the cilia are matted together, and pustules may develop. The conjunctiva usually shares in the inflammatory condition and there is a mucoid or purulent discharge. If the condition is untreated ulceration of the cornea may occur.

Treatment should be directed to finding if possible a cause for the condition, and by bathing the lids with an alkaline lotion containing sodium bicarbonate 0·5 per cent, and removing the scabs. When pustules develop, the cilia which project from them should be pulled out with cilia forceps, and the borders of the lid should be painted with 2 per cent silver nitrate solution. A mild antiseptic ointment should

be applied at night, such as one containing ammoniated mercury 2 per cent.

4.–STYES AND MEIBOMIAN CYSTS

476.] By the laity all localized swellings of the lids are called styes. In ophthalmic text-books there are a number of confusing names which must be mentioned. There are external styes and internal styes.

External stye   The external stye or hordeolum externum is a suppurative inflammation of one of Zeiss's glands. There is at first a small painful swelling, and later the whole lid may become oedematous. An abscess forms which generally points near the base of one of the cilia. Treatment should consist in the application of hot compresses and, when an abscess points, by opening it with a small knife. When successive crops of styes
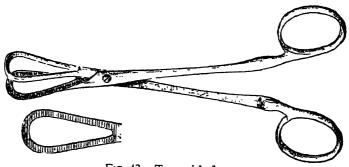
FIG. 43.—Traquair's forceps

occur the general health requires attention, particularly with regard to the presence of tonsillar or oral sepsis. In such cases the application nightly of an antiseptic ointment, such as ammoniated mercury 2 per cent, may reduce liability.

Internal stye or Meibomian cyst   The internal stye is an affection of a Meibomian gland. It is also called Meibomian cyst or tarsal cyst. It may be acute or chronic.

Acute   The acute internal stye, also called hordeolum internum or suppurating Meibomian or tarsal cyst, appears as an inflamed swelling in the tarsus which, being composed of dense fibrous tissue, does not yield easily, so that severe pain is caused. Treatment may be by everting the lid, making a crucial incision into the stye on the conjunctival surface, and evacuating its contents with a little curette. The following procedure is preferable as recurrence is entirely prevented. The conjunctiva is anaesthetized by four applications of a solution of cocaine hydrochloride 4 per cent, then the area surrounding the stye is infiltrated with a solution of procaine hydrochloride (novocain) 1 per cent, and ten minutes are allowed to elapse. The stye is then included between the blades of Traquair's forceps (see Fig. 43), an incision is made into the cyst with a small scalpel, the cyst wall is seized with toothed forceps, and with fine scissors the whole of the posterior wall of the cyst is removed. The

interior is scraped out with a curette, and a drop of pure liquefied phenol is applied to the interior of the pre-existing cyst. The eye is bandaged for two hours, or until all bleeding has ceased. After this the bandage is removed and the eye is bathed with boric acid lotion. By this means the cyst can never recur. Rarely a small granulation appears after a week or so at the site of the former cyst; this should be snipped off with scissors.

The chronic internal stye, also called chalazion, Meibomian cyst, or tarsal cyst, is formed by the replacement of the gland tissue of a Meibomian gland by granulation tissue. It may persist for a long time unchanged, it may undergo absorption, or it may become inflamed. Treatment should be that just described for acute internal stye. *Chronic Meibomian cyst*

5.–NEW FORMATIONS

477.] Milium is a retention cyst of a sebaceous gland, situated just below *Milium* the skin; it does not cause any trouble, but is unsightly. The contents may be evacuated by pressure, or enucleated with a small sharp curette.

Molluscum contagiosum is a small rounded tumour, the surface of *Molluscum contagiosum* which is somewhat flattened and has an umbilicated depression in its centre. On pressure a substance resembling sebum is discharged. The condition is contagious. Treatment is by ablation with a curette.

Xanthelasma is characterized by the appearance of a yellowish-brown *Xanthelasma* flat tumour on the upper or lower lid towards the internal angle of the orbit. There may be symmetrically placed tumours on all four lids. They do no harm, but may be removed for cosmetic reasons.

Rodent ulcer and epithelioma may occur at the lid margin, or at the *Rodent* inner angle of the orbit where the skin of the face joins that of the nose, *ulcer and epithelioma* or where skin is continually being rubbed by the frames of spectacles, especially pince-nez.

Rodent ulcer is less rapid in growth than epithelioma and cannot always be clinically distinguished from the latter. It begins as a tiny hardness of the skin, which develops a rolled edge, and may ulcerate. Although usually of slow development the condition may acquire increased malignancy and so should invariably receive early attention. On no account should any caustic be applied or any curetting be employed. In an early stage rodent ulcers are cured by the application of radium by a medical man who has experience of its use. Extirpation by the knife is more certain in its results so long as care is taken that the whole growth is removed.

6.–ANOMALIES OF POSITION

478.] Spastic entropion is an inversion of the lower lid in elderly people *Spastic* due to spasm of the orbicularis muscle (see Fig. 44). Its first appearance *entropion*

is often after the application of a bandage over the eye. Friction of the eye-lashes on the cornea may result in ulceration. In slight cases it may be prevented by the application of a strip of adhesive strapping to the skin of the lower lid and cheek which prevents inversion. In other cases a minor operation is required (see p. 246).

Senile ectropion
Senile ectropion of the lower lid is due to laxity of the fibres of the orbicularis muscle. The slackening of this muscle prevents the due apposition of the lower lacrimal punctum to the globe, so that drainage from the conjunctival sac is defective with resulting epiphora. There is no permanent cure for the condition except by a minor operation.
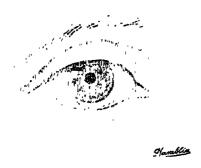
Trichiasis

Trichiasis is a new growth of lashes which are ill-placed. They are directed backwards and rub on the eye. Their friction on the cornea may result in ulceration of the cornea. The condition may be due to a cicatrix, or to hyperaemia of the lid margin due to chronic conjunctivitis. Trichiasis resulting from trachoma will be considered later. When there are not more than four or five ingrowing lashes the treatment should be by electrolysis or diathermy, which destroys the root-bulbs and prevents any recurrence. Epilation of the in-growing lashes can be carried out by anyone, even by the patient, but they will certainly grow again. When the number of in-growing lashes exceeds four or five a minor operation should be performed to alter their direction.

FIG. 44.—Spastic entropion

Trichiasis-entropion
Trichiasis-entropion resulting from trachoma has a double origin. First, the chronic inflammation of the conjunctiva is shared by the tarsus, with thickening of this boat-shaped fibrous structure; this results in an exaggeration of the inward curve of the tarsus, causing the lashes to approximate to the cornea, or even to rub on it. Second, the hyperaemia of the lid margin causes budding from the normal hair follicles; these new lashes are directed backwards and rub on the cornea.

On no account should epilation be performed except as a temporary expedient; operation for the relief of the condition is essential (see p. 248).

7.—SYMPTOMATIC CONDITIONS

Renal disease
479.] Oedema of both eyelids, more marked in the morning, suggests the necessity of examining the renal function.

Goitre
Proptosis or exophthalmos (see p. 43), palpebral fissures somewhat wider than normal, and a lagging behind of the upper lids when the eyes are directed downwards are among the signs of exophthalmic goitre (see p. 611).

Monocular proptosis or exophthalmos may be significant of an orbital tumour. *Orbital tumour*

Pulsating exophthalmos is generally due to an arteriovenous aneurysm, the communication being between the internal carotid artery and the cavernous sinus. *Arteriovenous aneurysm*

Swelling of the lids with proptosis and defective ocular movement is due to orbital cellulitis. *Orbital cellulitis*

8.—NERVOUS DISORDERS

480.] Blepharospasm is a spasmodic closing of the eyelids, seen typically in phlyctenular ulceration of the cornea, the result of contraction of the orbicularis muscle. It may persist in the dark. It may be overcome by thorough anaesthetization of the conjunctiva and cornea with solution of cocaine hydrochloride 4 per cent. Occasional clonic contractions of a few fibres of the orbicularis may be a sign of an uncorrected error of refraction. *Blepharo-spasm*

Acquired ptosis due to third nerve paralysis is usually unilateral: when occurring in myasthenia gravis it is usually bilateral. Ptosis may also result from injury. In all cases of ptosis the usual tests for syphilis should be made as a preliminary, after which the attention should be directed to the examination of the central nervous system. *Ptosis*

Lagophthalmos is a condition in which the eyelids do not completely close, especially during sleep. This may be due to shortening of the lids from injury or disease, or to paralysis of the orbicularis. The treatment should obviously be directed towards the cause of the condition. In severe cases, as when the cornea is exposed during sleep. it may be necessary to unite the lids by sutures. after rawing them, blepharorrhaphy (see p. 247): in slighter cases the cornea and conjunctiva may be protected by the instillation of castor oil. *Lagophthalmos*

Herpes zoster ophthalmicus is the result of an inflammatory affection of the Gasserian ganglion of the fifth nerve. It is characterized by the appearance of a crop of vesicles on the area of skin supplied by the supra-orbital branch of the frontal trunk of the ophthalmic division of the nerve (see Fig. 45). Prior to the appearance of the vesicles there is often severe pain in the area to be affected. Local treatment is by the application of some inert powder. On no account should any ointment be used. Pain should be relieved by the administration of analgesics; it may be so severe as to call for the use of morphine. *Herpes*

FIG. 45.—Herpes zoster ophthalmicus

9.—TROPICAL CONDITIONS

Phthiriasis 481.] Phthiriasis palpebrarum is an infestation of the cilia with the crab louse, *Phthirus pubis*. The black nits are seen adhering to the cilia. The condition is easily cured by rubbing the lids with ointment of ammoniated mercury 2 per cent.

Myiasis Myiasis is an infestation of the skin and subcutaneous tissue with the larvae of various flies, of which the most common is *Wohlfahrtia magnifica*. Unless the condition is treated at an early period the whole orbit may be infested with a horrible mass of stinking larvae. Treatment is by removal of all larvae, and by antiseptic applications (Wahba). (See also ARTHROPODS AND DISEASE, Vol. II, p. 124.)

Trachoma Cicatricial results of trachoma are only seen in their more serious aspect in trachomatous countries. To outline a typical case: both eyelids are inverted, with a new crop of cilia to the ocular side of the normal row; the tarsus is greatly thickened; the cornea is partially opaque with numerous vascular channels lying under the epithelium; there is a considerable amount of muco-purulent discharge from the eye. Operative measures are immediately required in such cases; epilation should not be employed.

10.—OPERATIONS

482.] Only such operations are here described as may have to be performed by any surgeon with operative experience.

Instruments for suturing Small curved needles are required, and fine black ophthalmic silkworm gut for skin sutures and fine silk for suture of the conjunctiva.

Spastic entropion of lower lid For spastic entropion of the lower lid, the instruments required are a scalpel, toothed forceps, entropion spatula, and scissors. Anaesthesia is produced by 4 per cent cocaine hydrochloride drops, and infiltration with 1 per cent procaine hydrochloride (novocain) solution containing adrenaline.

A horizontal incision is made 2 millimetres below the lashes throughout the whole length of the lid, which is made tense on the spatula; as much of the fibres of the orbicularis as can be seen is removed with scissors; any thickening of the tarsus should be shaved down; if there is any redundant skin a narrow strip may be removed from the lower skin edge, but this is not an essential part of the procedure; the edges of the wound are then united by a few sutures.

Canthoplasty and canthotomy For canthoplasty, the instruments required are a speculum (see Fig. 46), toothed forceps, strong scissors, and narrow scissors.

The speculum is inserted, one blade of a pair of strong scissors is thrust horizontally outwards into the conjunctival sac, the other blade being outside the skin, and the external canthus is divided. An additional cut with the smaller scissors is then made into the connective-tissue strands which attach both lids to the edge of the orbit, so that each is freely

movable and may be readily separated from the other. If only a temporary widening of the palpebral fissure is desired, nothing further is necessary and the wound soon closes. This operation, canthotomy, is all that is required in most cases of conjunctival oedema, the result of purulent inflammation.

If, however, a permanent result is required the conjunctiva must be undermined towards the cornea. Two or three sutures are then intro-

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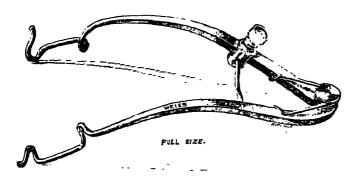
FIG. 46.—Eye speculum

duced to draw the conjunctiva up to the skin wound. This is the operation of canthoplasty.

For blepharorrhaphy, the instruments required are a scalpel, which *Blepharo-* should be small and sharp, toothed forceps, entropion spatula (see *rrhaphy* Fig. 47), and scissors.

The spatula is placed beneath the upper lid, which is made tense thereon. An intermarginal incision into the free border of the lid just

WEISS
FULL SIZE

FIG. 47.—Entropion spatula

behind the lashes, about 1·5 millimetres deep, is made without injuring the hair follicles. The same procedure is carried out on the lower lid. The rawed surfaces are then united by sutures. The whole or part of the lids can be thus united. When carefully performed the union is permanent until reopened by subsequent operation, after which no deformity remains.

For grattage in the second stage of trachoma with gelatinous follicles *Grattage* or with hypertrophied papillae, the instruments required are Graddy's forceps (see Fig. 48), a sharp spoon, and a lid-retractor.

A general anaesthetic is required for children. For others local anaesthesia is obtained by infiltrating the lids with 1 per cent procaine hydrochloride (novocain) solution and instilling drops of 4 per cent cocaine hydrochloride solution five times, after which the conjunctiva

should be thoroughly bleached by the application of adrenaline hydro-chloride solution, 1 in 1,000; ten minutes must be allowed to obtain the full action of the anaesthetic.

The upper lid is everted and Graddy's forceps are applied to the everted conjunctiva and withdrawn, carrying in front of their concavity the gelatinous contents of the follicles which are ruptured by the passage of the instrument. If follicles are present in the fornical conjunctiva, the retrotarsal fold should be seized with a pair of toothed forceps in order to allow the lid to be re-everted; the fornix is then curetted. After restoring the lid to its ordinary position it should be everted onto the
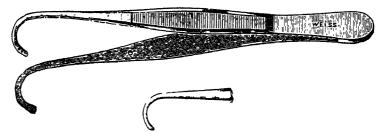
FIG. 48.—Graddy's forceps

lid-retractor and the conjunctiva should be curetted. The lower lid should be curetted, since unless the conjunctiva is loose Graddy's forceps are not always applicable.

Mercuric chloride solution 1 in 500 is then applied to the bleeding conjunctiva by means of a pledget of good quality cotton-wool wound round a glass rod.

Subsequent treatment is by the daily application of the same solution of mercuric chloride. This operation is required in every case of the second stage of trachoma, previous to other forms of treatment.

Other operations for trachoma   Full details of the various operations recommended for trichiasis and entropion resulting from trachoma were given by MacCallan, 1925. One of these, Streatfeild's operation, sometimes known as Snellen's operation, will be described here.

Streatfeild's operation   The instruments required are an entropion spatula or a metal shoe-horn, a scalpel, a toothed forceps, a needle holder, and some black ophthalmic silkworm gut.

The operation is carried out under local anaesthesia obtained by infiltra-tion of the lid with 1 per cent procaine hydrochloride (novocain) solu-tion containing adrenaline hydrochloride, and the instillation of drops of 4 per cent cocaine hydrochloride solution. The spatula is inserted under the lid and a horizontal incision is made through the skin 4 millimetres above the lashes. The upper edge is undermined for 2 milli-metres; the lower edge is undermined as far as the lashes. The orbicularis is cleared away from the tarsus. A wedge-shaped strip of cartilage is removed from the whole horizontal extent of the thickened tarsus in one strip, thus: an incision 0·5 millimetre deep perpendicular to the tarsus is made just above the roots of the lashes. An oblique incision is then made 2 milli-

metres above the first incision and the wedge included between the two incisions is then removed, its base being between the two incisions. A thin layer of tarsal tissue only intervenes between the apex of the wedge and the palpebral conjunctiva. Removal of the wedge is begun from the outer side in each eye. If the whole cartilage is greatly thickened it may be shaved down. The sutures are now inserted. The needle must be entered through the lower skin-flap near to but above the lashes, and in front of the cartilage. A horizontal bite of the cartilage close above the groove formed by the removal of the wedge is taken with the needle, which is returned through the lower skin flap 3 or 4 millimetres from its entrance. Four such sutures are inserted: the tarsus being deficient near the inner canthus, the horizontal bite is taken through the soft tissue which replaces it, as high up as possible. The wound is washed free of blood and the sutures are tied by a single knot with a double turn so as to lie horizontally. In the first instance the sutures should be loosely tied, and adjusted later, their tightness being proportionate to the amount of eversion required. Excessive tightness causes strangulation and subsequent necrosis of the lid margin. The edges of the skin are drawn together with a continuous suture. A sterilized gauze dressing is applied and is not removed until the fourth or fifth day after the operation, when the sutures are removed and no further dressing should be required.

The border of the lid after healing has occurred will be thick and unsightly if any excess of cartilage is left below the wedge-shaped groove.

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FABISM

See HAEMOGLOBINURIA

FALLOPIAN TUBES
DISEASES

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Reference may also be made to the following titles:

1.–TORSION

483.] Torsion of the Fallopian (or uterine) tube is rare, but may occur *Signs and* if the mesentery is unduly long. The patient complains of sudden pain *symptoms* in one iliac fossa accompanied by nausea, sometimes by actual vomiting. Tenderness and muscular rigidity are present on the affected side of the abdomen, and vaginal or rectal palpation may reveal a tender swelling lying to one side of the uterus.

In the differential diagnosis acute appendicitis, ectopic pregnancy, and *Differential* torsion of a small ovarian or broad-ligament cyst require consideration. *diagnosis*

Appendicitis should present little difficulty, as the characteristic *From* symptom-sign sequence of epigastric or umbilical pain, nausea or vomit- *appendicitis* ing, and local iliac tenderness will usually be present and there will be no pelvic swelling.

Torsion of the pedicle of a small ovarian or broad-ligament cyst is *From torsion* difficult to exclude, but this is of little consequence, as similar treatment *of pedicle of* will be required, namely, early laparotomy and removal of the affected *cyst* structure.

2.–INFECTIONS

484.] Inflammation of the Fallopian tubes or salpingitis occurs as part of an infective process involving in greater or less degree the whole of the internal genital organs and pelvic peritoneum.

During menstrual life infections of the corporeal endometrium soon resolve, but the narrow lumen of the uterine end of the tube and the complicated arrangement of its mucous membrane interfere with drainage into the lower genital tract and favour the retention of inflammatory exudates and the spread of infection to the pelvic peritoneal cavity. In these respects the Fallopian tube is not unlike the vermiform appendix, but there the resemblance ceases, as there is not the same danger to life in salpingitis as in appendicitis.

Salpingitis may be due to: (1) gonorrhoea; (2) septic infection following *Causes* abortion or labour; (3) tuberculosis; or (4) extension from an infective lesion of the bowel.

(1)—Gonorrhoeal Salpingitis

Gonorrhoea is the most important cause of salpingitis and is said to be *Aetiology* responsible for 70 per cent of cases. Infection usually occurs during coitus, but occasionally infected clothing or toilet seats or even the examining fingers of a careless practitioner may be responsible.

The primary, and in many cases the sole, lesion is an acute inflamma- *Morbid* tion of the lower genital tract, but in certain circumstances the infective *anatomy* process may spread along the mucous surfaces to the body of the uterus, tubes, and pelvic peritoneum. The tubes become much swollen and congested and the mucous membrane acutely inflamed. Pus is poured into

the lumen and escapes through the fimbriated end into the peritoneal cavity, thus setting up an acute pelvic peritonitis. The abdominal ostium of the tube often becomes occluded by inversion and adhesion of the inflamed fimbriae with the formation of a haematosalpinx, pyosalpinx, or hydrosalpinx according to the virulence of the infection.

FIG. 49.—Double hydrosalpinx. (Figs. 49 to 55 from specimens in The Department of Obstetrics and Gynaecology, University of Manchester)

Permanent morbid changes in tube

When the disease has run its course and become quiescent, the permanent damage to the tube may be represented by a few adherent plicae not sufficient to interfere with patency, by complete obstruction of the lumen, or by gross changes in the form of hydrosalpinx or pyosalpinx (see Figs. 49 and 50).

(a) Acute Gonorrhoeal Salpingitis

Acute salpingitis may develop at any time after the initial attack of gonorrhoea, but the interval is rarely less than three weeks.
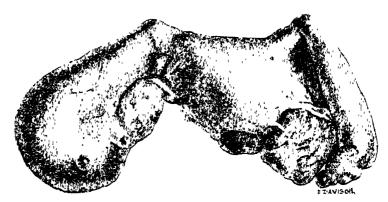
FIG. 50.—Double pyosalpinx

Clinical picture

Severe pain diffused over the lower abdomen is the first symptom, and in the case of a woman known to be suffering from gonorrhoea is conclusive evidence that the Fallopian tubes have become involved. Vomiting is usually absent. The temperature rapidly rises to 102° or 103° F., and the pulse is proportionately increased. There may be a feeling of chilliness, but rigors are uncommon. These symptoms often

coincide with a menstrual period, or the period may come on prematurely: in either event the loss of blood is usually excessive.

The lower abdomen is extremely tender on palpation, and there is *Examination* considerable muscular rigidity. Careful examination of the vulva may *of patient* reveal evidence of urethritis, Bartholinitis, or purulent vaginal discharge. Vaginal examination is usually unsatisfactory because of extreme tenderness of the pelvic organs, but in some cases it may be possible to feel the enlarged tubes or even a collection of pus in the pouch of Douglas.

Acute symptoms last about a week and then gradually subside, but if *Course and* pus forms pyrexia may persist longer. Recurrent acute attacks are not *prognosis* uncommon and are due to reinfection from the lower genital tract. Recovery from the acute attack may be complete, or some symptoms may persist or develop as a result of permanent damage to the affected structures.

Lower abdominal pain, pyrexia, and tenderness on abdominal and *Diagnosis* vaginal examination, especially if associated with a history of acute infection of the lower genital tract or purulent vaginal discharge, strongly supports a diagnosis of acute salpingitis, but the specific diagnosis of gonorrhoea should only be made after positive smears have been obtained from the urethra.

In the differential diagnosis the chief bugbear is acute appendicitis, *Diagnosis* and many cases are sent into hospital with that diagnosis; but in appendi- *from* citis the symptom-sign sequence mentioned on page 251 is usually present *appendicitis* and there are no symptoms or signs pointing to a pelvic lesion.

In pyelitis the temperature is higher and rigors are more frequent. The *From* pain is usually referred to the loin, and the affected kidney is tender on *pyelitis* pressure. The urine is acid and contains pus and coliform organisms.

As an infected husband may transmit the disease to his wife after all *Treatment* symptoms have disappeared, protected intercourse should be insisted on until repeated bacteriological examinations have shown him to be free from infection.

Acute gonorrhoea will usually remain localized in the lower genital tract if the parts are kept at rest and active local treatment is avoided as far as possible.

When acute salpingitis has developed, treatment should be expectant. The truth of this statement has been demonstrated again and again, and practically all gynaecologists are in agreement. Unfortunately a few general surgeons still believe that immediate laparotomy is necessary as the tubes may rupture and general peritonitis ensue. Such an accident is extremely rare; gonorrhoeal salpingitis and peritonitis almost invariably remain localized in the pelvis. Active surgical treatment results in a much higher mortality and also interferes with the complete recovery of the diseased structures, which occurs in a considerable percentage of cases. In America, where the term 'hot tubes' is applied to acute salpingitis, C. J. Miller has demonstrated that 90 per cent of the mortality is associated with operations undertaken before the tubes have 'cooled'. Moreover, a follow-up of cases treated expectantly has

shown that there is a 10 to 12 per cent chance of subsequent pregnancy, a possibility which immediate operation eliminates to a very large extent if not entirely.

General treatment   The patient with acute salpingitis should receive general care as for any acute infection, i.e. complete rest, free elimination, plenty of fluids, light nourishing diet, and adequate sleep. Pain should be relieved by hot applications to the lower abdomen and, if sedatives become necessary, diamorphine hydrochloride (heroin) in doses of $\frac{1}{12}$ to $\frac{1}{6}$ grain may be given as required.

Drainage of abscess   The presence of pus does not necessarily call for surgical interference, as many cases do better if left alone; but if an abscess points in the pouch of Douglas it should be drained through the posterior fornix.

(b) Chronic (Persistent) Gonorrhoeal Salpingitis

Subsidence of the acute attack may be followed by disappearance of all symptoms and even by complete restoration of function, but such a happy result is not to be expected in every case, and surgical intervention may be required later for the relief of symptoms due to the residues of infection.

Clinical picture   In such cases there may be recurrent acute attacks, or the patient may complain of chronic pelvic pain, dysmenorrhoea, menorrhagia, or persistent discharge. On examination the uterus will probably be retroverted and adherent, or definite adnexal swellings may be present.

Diagnosis   Diagnosis will be based mainly on the history of an acute attack of salpingitis; if this cannot be obtained, pelvic endometrioma and ectopic pregnancy (see p. 258) may have to be excluded.

From endometrioma   Endometrioma is a new growth which usually develops in the ovary or pouch of Douglas and causes enlargement and fixation of the pelvic organs. One or both ovaries may be cystic and adherent, there is reduced mobility of the uterus, and shotty nodules may sometimes be palpated through the posterior fornix. The presence of these physical signs in a patient whose menstrual periods have recently become painful is strong evidence in favour of endometrioma.

Treatment   Treatment may be required for recurrent attacks of acute salpingitis, chronic ill health, or sterility.

Recurring acute attacks may be prevented or minimized by instructing the patient to avoid prolonged or violent exercise and excessive or unprotected sexual intercourse, but if these precautions are impracticable it will be necessary to remove the damaged tubes and uterus.

Similarly, patients who complain of chronic pelvic pain, menorrhagia, and dysmenorrhoea may be kept in a reasonable state of health by relieving pelvic congestion and prescribing hydrotherapy and adequate rest, but here again the restrictions may prove so irksome that surgical treatment is preferred.

Operation   Operative procedures should be postponed until the disease has become quiescent, as shown by absence of pyrexia for two weeks or a blood sedimentation rate of at least an hour. As regards the scope of

the operation, Curtis is of opinion 'that surgery, when resorted to, should be directed to reconstruction of tissues laid waste by disease rather than to removal of organs for the purpose of stamping out infection'. No doubt this is the ideal to be aimed at, but considerable difference of opinion exists regarding to what extent it is possible to repair seriously damaged organs and yet to ensure complete disappearance of the symptoms complained of. A patient who submits herself to a serious abdominal operation naturally expects to be cured; it is therefore essential that the surgeon should temper his conservatism with common sense and not overlook this fact.

When sterility is complained of it is necessary to make a complete *Treatment of sterility* examination of both husband and wife. The husband's semen should be examined for live and active spermatozoa, and if the result is satisfactory the woman's Fallopian tubes should then be tested for patency by Rubin's method of transuterine insufflation. If any obstruction is found it is possible to determine its situation and extent by radiological examination of the pelvic cavity after introducing lipiodol into the uterus. A word of caution is necessary about both procedures, as insufflation may drive infective material into the upper genital tract if the disease is not quiescent and lipiodol may occasionally act as an irritant and damage the tubal mucous membrane.

Operative procedures for the restoration of tubal patency are steadily improving, but have not yet reached a stage when it is possible to promise more than a 10 per cent chance of subsequent pregnancy. Under these circumstances it is unwise to recommend operations of this character unless the patient, in her anxiety to become pregnant, is determined to try every possible method.

(2)—Septic Infections following Abortion or Labour

The organisms chiefly concerned in these infections are certain groups of haemolytic streptococci, and the lesions produced differ considerably from those met with in gonorrhoea. The infection does not spread along the mucous surfaces but penetrates the uterine wall or gains access to the pelvic cellular tissue through a laceration. In either event further extension is by the lymphatics or pelvic blood-vessels, and the Fallopian tubes are involved from without, a perisalpingitis rather than an endosalpingitis being the result (see Fig. 51).

Pelvic peritonitis is severe, and the resulting adhesions are dense and cause much distortion of the affected organs. The tubal mucous membrane, however, often remains intact, so that when surrounding adhesions have been separated complete restoration of function is possible.

The clinical features are similar to those of gonorrhoeal salpingitis, but *Clinical picture* as the organisms are more virulent there is greater danger to life. The temperature is usually higher, and rigors occur more often.

The differential diagnosis from gonorrhoea will rest mainly on a history *Diagnosis from gonorrhoea* of recent abortion or labour, but brawny exudates and local injuries are in favour of septic infection, and abscess formation is commoner.

Treatment   Acute cases should be treated expectantly and immediate surgery only resorted to when pus forms. Surgical treatment of the sequelae will usually be radical because of the dense adhesions and extensive damage

FIG. 51.—Septic salpingitis

to the affected organs, but in less severe cases conservative operations for the relief of sterility are more successful than in gonorrhoea.

(3)—Tuberculosis

Tuberculosis has a marked preference for the Fallopian tubes, but the body of the uterus, particularly the cornua, is also affected fairly often, and in severe cases the ovaries may also be involved.

Source of infection   There may be a primary focus in the lungs or elsewhere, but in the majority of cases the genital lesion is the only one that is active. There are three possible avenues of infection, the blood-stream, the peritoneal cavity, and the lower genital tract; of these the first is undoubtedly the most important.

Age incidence   The disease may occur at any age, but as tuberculosis often remains latent for long periods it is probable that many patients who develop symptoms in later life have actually been infected during childhood or adolescence. In such cases a smouldering lesion has burst into flame, and this event may be precipitated by the establishment of menstruation, the beginning of married life, or the occurrence of pregnancy, labour, or abortion. Occasionally, however, the acute exacerbation is the result of a superimposed infection derived from the bowel, or possibly gonococcal.

Morbid anatomy   The lesions produced may be fibrotic, caseous, or purulent. In the fibrotic type the tubes and cornua are much thickened and the uterine fundus has a saddle-shaped appearance (see Fig. 52).

In the caseous and purulent types the tubes may be distended with pus and indistinguishable except by histological examination from other kinds of pyosalpinx.

Sequelae   As the fimbriated ends of the tubes frequently remain open, infective material may escape into the peritoneal cavity and set up a tuberculous

peritonitis; many cases of tuberculous peritonitis arise in this way and are characterized by glueing together of the coils of small intestine below the level of the umbilicus. Pelvic adhesions are usually dense and very extensive, and the ovaries are frequently converted into abscesses.

The symptoms are not characteristic but are those common to other *Clinical* varieties of salpingitis. The disease, however, tends to be subacute or *picture* chronic and is markedly resistant to the ordinary forms of palliative treatment.

The onset is often insidious, but may be fairly acute with moderate pyrexia, increased pulse-rate, and general malaise. Menstrual disturbances are common, menorrhagia, dysmenorrhoea, and sometimes amenorrhoea. Tenderness and rigidity are present in the lower abdomen,

FIG. 52.—Tuberculous salpingitis, fibrotic type

and on vaginal examination definite enlargement and fixation of the appendages will usually be found.

The acute stage soon subsides, and the patient then complains of chronic pelvic pain, backache, menstrual irregularity, and leucorrhoea.

A history of tuberculosis during childhood, a family history of tuber- *Diagnosis* culosis, or the presence of a tuberculous lesion elsewhere are significant points in diagnosis. Salpingitis in virgins is also most likely to be tuberculous.

When amenorrhoea is one of the symptoms and pregnancy can be *Aschheim-* definitely excluded, the Aschheim-Zondek test may be helpful, as it is *Zondek test* often positive in such cases (Wilson). A definite diagnosis, however, is only possible after the diseased tubes have been removed and submitted to histological examination.

Expectant treatment is indicated during the acute stage, but later, when *Treatment* gross changes are present, surgical treatment will usually be necessary unless there is an active lesion in the lungs.

Operation should be radical and comprise removal of uterus, tubes, *Operation* and ovaries, as it is rare for the disease to be limited to the Fallopian tubes. The end-results are quite good, as 70 per cent of the patients are alive and well after a considerable number of years.

During convalescence it is advisable to prescribe a course of sanatorium or similar treatment.

As an alternative to surgery X-ray therapy has been recommended and is widely used in Germany. Jameson advocated this method and referred to a series of 169 cases, 80 per cent of which showed definite improvement.

(4)—Extension from Infective Lesions of Bowel

The close relations of the vermiform appendix and the right Fallopian tube make it possible for the latter to be involved in acute appendicitis, but, as the bowel symptoms dominate the clinical picture, the tubal lesion is of secondary importance. Later on, however, the patient may complain of unilateral pelvic pain, and this symptom, taken in association with an adherent right appendage and a history of previous appendicitis, will point to a correct diagnosis. Treatment consists in removal of the diseased structures.

Diverticulitis   In diverticulitis there will usually be a long history of recurrent pain referred to the left iliac fossa and tenderness over the pelvic colon with perhaps some muscular rigidity on the left side. A sausage-shaped swelling may be felt lying above and parallel to the inguinal (Poupart's) ligament or occupying the left posterior quadrant of the pelvis. When the infective process has involved the left ovary and tube the important points in diagnosis will be the history of symptoms referable to the colon, and the posterior situation of the pelvic swelling.

Treatment is difficult but should be expectant unless an abscess forms.

3.—TUMOURS OF THE FALLOPIAN TUBES

Primary carcinoma   485.] New growths of the Fallopian tubes are rare. Primary carcinoma is the most important and forms a tumour about the size of a pigeon's egg. Diagnosis is very difficult, but a watery sanious discharge associated with a distinct and tender swelling in one lateral fornix, without clear evidence of infection, uterine cancer, or a movable ovarian tumour would be in favour of the condition (Alban Doran).

4.—TUBAL PREGNANCY

(1)—Aetiology and Clinical Picture

486.] The aetiology of tubal pregnancy is not fully understood, but a preceding salpingitis is undoubtedly the most important factor, as there is evidence of this in nearly 50 per cent of cases (Dougal). A uterine decidua is formed in every case, but the decidual reaction in the tube is imperfect; this, together with the thin muscle wall, no doubt accounts for the frequency with which haemorrhage into the ovum and tubal abortion or rupture occur.

Tubal abortion and rupture   The foetus rarely survives for more than a few weeks, and a blood mole is usually formed quite early. The ovum is expelled into the lumen

of the tube, where it may remain for a time or be immediately discharged through the abdominal ostium (tubal abortion) or a rent in the wall of the tube (tubal rupture) into the abdominal cavity, these happenings being accompanied by a variable amount of haemorrhage into the abdominal cavity (haematocele). Occasionally the tube wall ruptures between the folds of the broad ligament, and a broad ligament haematoma results.

After abortion or rupture the attachments of the ovum are usually completely destroyed, but in a few cases this is not so and the foetus may survive, even to term, in its new situation (secondary abdominal or intraligamentary pregnancy). A still rarer event is for the foetus to reach maturity in the Fallopian tube. When the foetus dies the uterine decidua is separated and expelled as a cast; this is accompanied by a certain amount of uterine haemorrhage.

The diagnosis of tubal pregnancy is based on a complex made up of *Clinical* one or more of the three cardinal symptoms, amenorrhoea, uterine *picture* haemorrhage, and abdominal pain, together with certain physical signs produced by enlargement of the Fallopian tube and intraperitoneal haemorrhage.

Amenorrhoea is found in over 70 per cent of cases but rarely exceeds *Amenorrhoea* two months; in most cases the patient has merely gone a week or two 'over' her period.

Uterine haemorrhage is present in more than 80 per cent of cases and *Uterine* indicates that the ovum has been damaged. The haemorrhage is almost *haemorrhage* invariably moderate in amount without clots, dark in colour, and persistent. To begin with, the bleeding is associated with separation and expulsion of the uterine decidua, but it continues after the decidua has been expelled and even after the uterine cavity has been curetted. Its continuance is probably due to some hormonal stimulus exerted by chorionic villi still alive in the tube and is therefore comparable to the bleeding found in incomplete abortion. This view is supported by the fact that haemorrhage ceases as soon as the gravid tube has been removed.

Abdominal pain is present in practically every case and varies in severity *Abdominal* from the colicky pain associated with a gestation still in the tube to the *pain* acute lancinating pain met with in tubal rupture. To begin with, the pain is unilateral and referred to the region of the affected tube, but later it may become diffused over the lower abdomen.

All three cardinal symptoms are present in over 60 per cent of cases, the usual order of their occurrence being amenorrhoea, abdominal pain, and uterine haemorrhage.

Two other symptoms which deserve special mention are pain on defaecation and shoulder-tip pain. The gravid tube and adjacent parietal *Pain on* peritoneum form a sensitive area which is irritated during defaecation, *defaecation* and the resulting pain is usually sufficiently severe to attract the patient's attention. Shoulder-tip or 'epaulette' pain is produced by irritation *'Shoulder-tip'* of the sensory branches of the phrenic nerve supplying the diaphragm *pain*

and is complained of when diffuse intraperitoneal haemorrhage has occurred.

Physical signs   The physical signs are best considered in relation to the different clinical types to be described presently, but there are two special signs which may be referred to here.

Cullen's sign   Cullen's sign (Smith and Wright) consists of a bluish coloration of the skin of the umbilical region and is caused by extravasation of blood into the connective tissue of the abdominal wall. How the blood gets into that situation is not quite clear, as the sign is not necessarily associated with gross intraperitoneal haemorrhage. The phenomenon is extremely rare and therefore of little value in diagnosis.

Salmon's pupillary sign   The same may be said of the pupillary sign described by Salmon, a unilateral dilatation of the pupil occasionally found in cases of diffuse intraperitoneal haemorrhage.
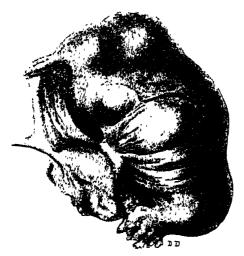
(2)—Clinical Types

As the clinical picture of tubal pregnancy is extremely variable, it is convenient to divide cases into four types as follows: (*a*) ovum still in the tube and little or no haemorrhage into the abdomen (13 per cent) (Dougal); (*b*) tubal rupture or abortion with diffuse intraperitoneal haemorrhage (28 per cent); (*c*) tubal rupture or abortion with encysted haemorrhage (60 per cent); and (*d*) advanced ectopic pregnancy (rare).

(a) *Ovum still in the Tube and Little or No Haemorrhage into the Abdomen*

Symptoms   The patient complains of colicky pain in one or other iliac fossa and often of irregular uterine haemorrhage, dark in colour and moderate in amount. She is not acutely ill and may even feel quite well except for the pain. There is usually some menstrual irregularity; in most cases the patient has gone a week or so over her period.

FIG. 53.—Unruptured tubal pregnancy— Type (*a*)

Examination of patient   Abdominal examination will yield little information except some tenderness on pressure over one iliac fossa. On vaginal examination the uterus may feel somewhat large if the decidual cast has not been expelled, and it may be possible to make out a tender elastic sausage-shaped swelling through one or other lateral fornix (see Fig. 53). The physical signs, however, are frequently inconclusive, and in such cases the patient should be examined under an anaesthetic.

(b) *Tubal Rupture or Abortion with Diffuse Intraperitoneal Haemorrhage*

This type (28 per cent) comprises the acute or urgent cases, of which *Symptoms* there are two varieties, the asthenic and sthenic. In the asthenic the haemorrhage prostrates the patient, and she will die unless treated as a surgical emergency; in the sthenic the bleeding is equally severe, but the patient reacts and, even if not operated on immediately, may recover from the acute attack. In the asthenic type of case the patient is seized with an agonizing and luncinating pain in the lower abdomen accompanied by extreme nausea and vomiting. Signs of internal haemorrhage rapidly supervene, feeble rapid pulse, shallow respiration

FIG. 54 —Ruptured tubal pregnancy—Type (b). A post-mortem specimen removed from a woman who died two hours after rupture. One tube has ruptured; the other is occluded as a result of preceding salpingitis. The uterus has been opened to show the decidua *in situ*

with frequent sighing, subnormal temperature, cold, clammy, and blanched skin, intense restlessness, and thirst.

On examination the abdomen is distended, and it may be possible to *Examination* demonstrate the presence of free fluid. Tenderness and rigidity are not *of patient* usually present, but there may be some resistance to pressure over the pelvic brim. On vaginal examination the affected tube may not be palpable, but there will usually be a fullness in the posterior fornix or even a doughy mass if the effused blood has clotted. (See Fig. 54.)

In the sthenic type the onset is similar, but the patient rallies in a short time. The pulse recovers its volume, and the temperature rises to 100° or 101° F. The skin is not usually pallid, and the mucous membranes are not blanched. The abdomen is distended and extremely tender on pressure; rectus rigidity is the rule and is usually more marked on the affected side. Shoulder-tip pain may be complained of. There is well-marked tenderness on vaginal examination and fullness or a doughy swelling in the posterior fornix as before.

(c) *Tubal Rupture or Abortion with Encysted Haemorrhage*

Symptoms   This is the commonest type (60 per cent) and includes the subacute cases. The patient complains of abdominal pain of moderate severity, usually in one or other iliac fossa but later diffused over the lower abdomen. Irregular uterine haemorrhage of the characteristic 'ectopic' type is almost invariably present and has usually followed a period of five or six weeks' amenorrhoea. A severe attack of pain followed by collapse may have occurred at an earlier date, or there may have been several less severe attacks accompanied by momentary faintness. Pain on defaecation is often complained of and occasionally dyspareunia. The patient looks ill, though not acutely so, and the skin may be slightly
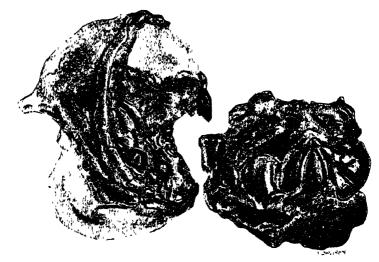
FIG. 55.—Tubal abortion—Type (*c*). The tube and ovary are shown with part of the wall of a peritubal haematocele. On the right is the extruded mole surrounded by adherent blood clot

jaundiced. The temperature is sometimes higher than normal, occasionally over 100° F.

Examination of patient   The abdomen is tender, especially on the affected side, but there is no rigidity. There may be resistance on pressure over the pelvic brim, or a definite tumour may be palpable. Vaginal examination will reveal a definite mass lying behind and to one side of the uterus, more rarely in front of it. (See Fig. 55.)

(d) *Advanced Ectopic Pregnancy*

In this type, a rare one, the pregnancy has usually continued beyond the fourth or fifth month, and in the majority of cases the tube has ruptured or aborted at an earlier period and a secondary abdominal pregnancy resulted. Abdominal enlargement, foetal movements, and foetal heart sounds may be observed as in the case of intra-uterine pregnancy, but the swelling is usually somewhat asymmetrical. Uterine contractions will not be elicited on palpation, and there may be some

Physical signs

difficulty in definitely outlining the 'tumour' because of spasm or rigidity of the abdominal muscles. On vaginal examination it may be possible to recognize that the foetal parts lie outside the uterus.

(3)—Course and Prognosis

The course and prognosis have been already indicated to some extent, and it will be realized that tubal pregnancy may present a clinical picture varying from a dangerous emergency to a chronic disability. With prompt diagnosis and treatment the prognosis is good, as most patients recover. In England and Wales there are about 80 notified deaths from ectopic pregnancy each year. The prognosis as regards subsequent pregnancies is also good, but there is a definite risk of another ectopic pregnancy occurring in the remaining tube.

(4)—Differential Diagnosis

Type (a)

In Type (a) appendicitis, threatened or incomplete uterine abortion, inflammatory tubal swellings, small ovarian or broad-ligament cysts associated with a uterine pregnancy, and metropathia present the greatest difficulties.

When the gestation is in the right tube the case may be diagnosed as *Diagnosis* appendicitis, but the symptom-sign sequence of appendicitis is absent *from appendicitis* and amenorrhoea and uterine haemorrhage, if present, definitely point to a pelvic lesion (see p. 251).

Threatened uterine abortion should present little difficulty. There will *From* be uterine enlargement corresponding to the period of amenorrhoea and *threatened uterine* possibly some dilatation of the cervix. Pain, if present, will be referred *abortion* to the hypogastrium or sacral region, haemorrhage will be more profuse and the blood of a brighter colour, and no extra-uterine swelling will be palpable.

Occasionally the decidual cast is mistaken for an early ovum, and the *From* bleeding which persists after its expulsion for that due to incomplete *incomplete uterine* uterine abortion. In ectopic pregnancy, however, the pain and haemor- *abortion* rhage are quite different, and a careful pelvic examination will reveal a small uterus and tender extra-uterine swelling. Histological examination of the cast may also be helpful, as it will show decidual cells but no chorionic villi.

Inflammatory tubal swellings of subacute or chronic type are usually *From* bilateral. In addition, there will be a longer history of ill-health, *inflammatory tubal* vaginal discharge will be present, and menstruation will be too frequent *swellings* and the loss excessive.

When a small ovarian or broad-ligament cyst is associated with early *From cysts* uterine pregnancy diagnosis may be more difficult, but if haemorrhage is present its character will afford a clue. In any case the uterus will be definitely enlarged and the extra-uterine swelling thin-walled, cystic, and not definitely tender.

From metropathia

In metropathia haemorrhagica ovulation does not occur and a corpus luteum is not formed. A follicular cyst develops in one ovary and, as a result of the excessive or prolonged action of oestrin, the proliferative phase of the menstrual cycle is exaggerated, the endometrium becomes polypoid, and blood oozes from it. The clinical picture may resemble that of ectopic pregnancy, as there is often an initial period of amenorrhoea followed by bleeding, some unilateral pain, and an enlarged and palpable ovary. The latter, however, is thin-walled and cystic and does not feel like a gravid tube.

Type (*b*)

Diagnosis from perforation

In Type (*b*) various acute abdominal catastrophes, such as perforation of the appendix, stomach, or gall-bladder, have to be excluded, but 'the history of the case, the sudden onset and the persistence of extreme pallor and subnormal temperature without rigidity of the abdominal wall, in a patient previously well except for some menstrual irregularity, seldom or never leave room for doubt' (Zachary Cope).

From acute salpingitis

The sthenic type of case may sometimes be mistaken for an acute salpingitis and treated expectantly for a time. Amenorrhoea followed by bleeding is occasionally found in these cases, and a correct diagnosis may have to be based on the short and characteristic ectopic history and the presence or absence of a purulent vaginal discharge or other symptoms pointing to a recent pelvic infection.

Type (*c*)

Cases belonging to Type (*c*) have to be distinguished from pelvic appendicitis, pyosalpinx or pelvic abscess, and retroversion of the gravid uterus.

Diagnosis from pelvic appendicitis

Pelvic appendicitis is particularly difficult to exclude, as it may closely resemble a small pelvic haematocele. In ectopic pregnancy, however, there will usually have been a short period of amenorrhoea, characteristic uterine haemorrhage will be present, the patient will appear somewhat anaemic, and a history of the initial attack of pain and faintness suggestive of intraperitoneal haemorrhage will generally be forthcoming.

From pyosalpinx and pelvic abscess

In pyosalpinx, on the other hand, there will be a longer history of ill-health and some evidence of previous pelvic inflammation.

Occasionally it is difficult to decide whether a mass in the pouch of Douglas is a haematocele or a pelvic abscess; in such cases it is permissible to puncture the posterior fornix with a needle and to withdraw

Aschheim-Zondek test in tubal pregnancy

some of the contents. The Aschheim-Zondek and Friedman tests are valuable aids to diagnosis when uterine pregnancy can be ruled out and it is possible to postpone treatment until the result of the test has been obtained. A positive reaction means that living chorionic villi are present, but a negative reaction does not rule out the possibility of a gestation which has become 'chronic'.

From retroverted gravid uterus

A retroverted gravid uterus should present no difficulty unless the tubal pregnancy has progressed to the third or fourth month. There

will be a history of three or four months' amenorrhoea with the characteristic appearance of bladder symptoms during the fourth month, and the other signs and symptoms of uterine pregnancy will be well marked. If a catheter is passed and the bladder emptied, the absence of the uterine fundus from its proper position will be noted.

Type (d)

In Type (*d*) diagnosis is extremely difficult, and there may be considerable delay before the true state of affairs is recognized.

The peculiar shape and position of the abdominal swelling may arouse suspicion, as may the fact that on vaginal examination it is possible to separate the uterus from it. Radiological examination of the abdomen may demonstrate that the foetal parts lie outside the uterus.

(5)—Treatment

The treatment of ectopic pregnancy is surgical *and the earlier operation is performed the better.*

In very acute cases, when shock is profound and the pulse imperceptible, the patient's general condition should be improved by means of blood transfusion or gum-saline infusion, but this should be done while preparations are being made for immediate operation.

The extent of the operation will depend on the condition of the patient. *Extent of* In serious cases nothing more should be done than is actually required *operation* to save life, and this generally means excision of the affected tube with or without the corresponding ovary. No time should be lost in removing blood from the peritoneal cavity, but if the patient is much exsanguinated some of it may be citrated and introduced into a vein, or the peritoneal cavity may be flooded with warm saline. When the case is subacute and the pelvic organs are disorganized or the seat of an old infective lesion, it is best to remove the diseased structures.

In advanced ectopic pregnancy great care is necessary in dealing with *Advanced* the placenta, as large uncontrollable blood sinuses may be opened if it *cases* is separated from its attachments. The safest plan is to leave the placenta *in situ* and to allow it to be absorbed.

Some advocates of conservative surgery recommend that the gravid tube should be saved whenever possible, but this is unjustifiable unless the other tube has already been removed or is hopelessly damaged.

The operations are carried out abdominally except in those rare cases of infected pelvic haematocele when it is best to evacuate the blood through the posterior fornix.

The results of operation are extraordinarily good. There is probably *Results of* no disease of equal severity in which the response to prompt surgical *operation* treatment is so rapid or satisfactory.

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FARCY

See GLANDERS, p. 555

FASCIOLIASIS

See FLUKE INFECTIONS, INTESTINAL, p. 320

FATIGUE, MENTAL

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Reference may also be made to the following title:

PSYCHONEUROSES

1.–DEFINITION AND SITES OF MENTAL FATIGUE

487.] Fatigue is usually defined as 'that state of lessened activity of an *Physical* organ which results from its previous activity'. But (i) so complex and *and mental fatigue* so wide-spread is the 'organ' of mind, (ii) so varied are the results of prolonged mental work, and (iii) so ignorant are we of the nature of mental activity that a correspondingly succinct definition of *mental* 'fatigue' is hardly possible.

In the first place, 'mental fatigue' in its widest sense may be due to *Causes of* changes anywhere in the nervous system, at the periphery, e.g. in the *mental fatigue* sensory end-organs, or centrally, e.g. in the cerebral hemispheres. And central 'fatigue' may be due to local conditions, e.g. to the waning of incentives or to the enfeeblement of drives, as in that 'state of lessened activity' known as 'boredom', in which the impairment that results from continued mental work in one particular field may be confined to that field, not extending to other fields of subsequent mental activity.

Or it may be due to general, perhaps toxic, conditions, in which case all higher mental activity is impaired whatever its nature, and the demand is no longer, as in boredom, for change of work but for rest from it.

Initial stimulating effect of mental work

In the second place, in some situations prolonged mental work may result in temporarily increased, not immediately in lessened, mental activity and in temporary feelings of excitement or even of exaltation, not immediately in feelings of weariness (M. Smith, 1916).

Mental fatigue as a state of exhaustion

In the third place, we might at first be disposed, on grounds of physiological analogy, to attribute mental 'fatigue' to the exhaustion of locally available mental 'energy'. But the only psychological evidence in favour of such a view of mental fatigue relates to structures outside the central nervous system, for example, the effects on consciousness produced by stimulating the 'protopathic' or 'spot' system of sensibility. These effects can be easily observed in the skin where the re-excitation of any one heat spot or cold spot immediately after its previous stimulation will fail to elicit a second sensation. Its previous response, comparable it has been supposed to an explosion, has apparently resulted in a complete exhaustion of available 'energy': rest is needed for its recovery.

2.–MENTAL FATIGUE AND ADAPTATION

Adaptation to colour and temperature stimuli

There are other sensations which do not show signs of such apparent exhaustion and in which the phenomena of 'adaptation' result from prolonged, or very rapidly repeated, excitation. For example, a not too intense colour stimulus, or a moderately warm or cool temperature stimulus, when continuously applied, ceases gradually and ultimately to give rise to a sensation of colour or of temperature. But this condition, if it can be usefully described under the general head of 'fatigue'— although, like 'boredom', it falls strictly under the accepted general definition of 'fatigue'—is peculiar in that if, when such adaptation has been established, a 'neutral' stimulus is substituted, i.e. a normally colourless stimulus, or a stimulus which is normally sensed as neither warm nor cold, an opposite or contrasting sensation at once develops—a green sensation if the previous stimulus had been red, a warm sensation if the previous stimulus had been cool. Clearly, the state of diminished and finally abolished reaction to the colour or temperature stimulus reached here is not one of exhaustion, but rather a balanced condition, at a particular level, of equilibrium between two antagonistic, contrasting, and mutually inhibiting processes, one now to a certain degree 'tired', the other better prepared for activity.

Adaptation to pleasure stimuli

It is noteworthy that an apparently similar 'adaptation' within the central nervous system ensues after prolonged subjection to conditions evoking moderate pleasure or displeasure. A kind of 'adaptation'—not a state of mere 'fatigue'—is at length established; the feeling-tone, say of displeasure, gradually disappears, giving place to a 'neutral' feeling-

tone (one neither of pleasure nor of displeasure); whereupon subjection to conditions which would normally have produced such a neutral feeling-tone evokes now, by contrast, presumably through the outweighing of one 'tired' process by its fresher antagonistic process, a feeling-tone of pleasure.

3.—MENTAL INDEFATIGABILITY

On the other hand, there are other sensations, if not too intense, or conditions of sensation, which seem virtually indefatigable. We can listen almost eternally, if we so attend, to the gentle ticking of a clock; we can endure, likewise without apparent sensory fatigue, the continuous daylight of a northern summer; we can similarly sit before and enjoy indefinitely the warmth of a winter fire. There are yet other prolonged, but more intense, sensations, e.g. the hearing of a continuous loud tone, which, while not suffering appreciable change themselves, nevertheless— owing it is believed to central inhibition rather than to fatigue (Rawdon-Smith)—result in a rise of the threshold of hearing for tones of the same and of neighbouring pitch.

So far as cerebral fatigue is concerned, we might at first sight wonder *Cerebral* whether any impairment of mental activity would be expected either *fatigue* through the exhaustion of locally available energy or through the local accumulation of toxic influences due to its expenditure—so abundantly nourished and so highly and continuously active appears to be the brain, and so minute seems to be the difference in its always intense metabolism, whether it is engaged in conscious mental work or is apparently at rest. There can, however, be no doubt that 'higher' mental fatigue is induced by the general diffusion of the toxins from focal sepsis and by toxins of muscular and intestinal origin.

4.—REFRACTORY PERIODS AND MENTAL FATIGUE

We might rather suspect the influence in the central nervous system of *Hypothetical* 'blocks' at the synapses, or of cumulative 'refractory phases' or other *'refractory* changes (Gerard and Marshall) analogous to those well recognized in *phases'* the peripheral nerve-fibres. But this supposition is negatived by the unlikelihood that, during prolonged mental work, precisely the same cerebral neurones are excited repeatedly by precisely the same rapidly recurring mental stimuli. Moreover, in the lower mammals at least, there is experimental evidence of a certain 'equipotentiality' of various regions of the cortex: e.g. it is the quantity, not the locality, of cerebral cortex destroyed that determines the degree of impairment of intelligent behaviour (Lashley). And in man it is probable that conscious processes, so far at all events as the higher levels of mental activity are concerned, involve the activity of very extensive areas of the brain functioning as

a whole, not so much the mosaic activities of narrowly localized regions of it. Indeed the notion of 'centres of consciousness' is fast becoming obsolete.

We may therefore well hesitate before associating mental fatigue with refractory phases and before ascribing, as some have ascribed (Bills; Telford), to refractory phases either (i) those numerous fluctuations, or even pauses, in mental activity which characterize prolonged continuous mental work, or (ii) the occurrence of an optimal rate of successive stimuli in order to obtain the fastest series of reaction times.

5.–FEELINGS OF FATIGUE

Effects of rest and sleep

Continuous concentration at any task becomes sooner or later impossible; it is our nature involuntarily or voluntarily to take repeated brief rests during any long period of mental work. But whereas the uninterrupted maintenance of mental activity in one particular field of attention cannot endure for long, the freer play of phantasy in daydreaming and in sleep seems untiring. Yet both rest and sleep, although neither involves mental quiescence, undoubtedly dissipate mental 'fatigue', whether such fatigue be estimated by our inward feelings or by such outward signs as skin colour, facial expression, or impaired output of mental work. It is noteworthy that our feelings of mental weariness are not invariably a faithful index of mental impairment: our lessened output of mental work may indicate that we are mentally fatigued without our necessarily feeling so, or we may feel mentally fatigued without necessarily showing it in poorer work. But in general it has been found experimentally that the diurnal variations from hour to hour in our feelings of mental fatigue during normal work-a-day life show certain striking resemblances to the fluctuations in output hourly obtained under these conditions (Muscio, 1921).

Measurement of mental fatigue

Measurement of the output of work is at present our most trustworthy index of its impairment due to mental 'fatigue'; for unfortunately we have no sufficiently reliable objective 'tests' of mental fatigue. Purely physiological tests have proved of little use. Periodically interpolated mental tests are at the mercy of the will and of the feelings of the subject; they are also subject to the effects of practice and of consequent automatism; and they differ owing to their necessary simplicity from more complex, directive, aim-satisfying higher mental work. Despite these and other drawbacks, there can be no doubt that in general the efficiency of performing certain interpolated mental (e.g. arithmetical) tests is lowered by continuous mental work. As judged by the diminishing capacity to perform these tests, there is no clear evidence that mental 'fatigue' is uniformly progressive throughout a day's ordinary work. Moreover, diurnal variations in degree of fatigue seem to be superimposed on an independent organic rhythm of mental efficiency; for whether the day is spent in ordinary mental work or in such restful

occupations as sitting or chatting, similar, although less marked, variations in the efficient performance of interpolated tests occur throughout the day (Muscio, 1920).

6.–PATHOLOGICAL MENTAL FATIGUE

Feelings of ·physiological' mental fatigue, i.e. of fatigue which is effect- *Normal variations in fatigability* ively dispelled by comparatively brief rests or by sleep, show vast individual differences. At the one extreme there are the very rare mental athletes (I am acquainted with one of them) who assert that apart from passing boredom or worry they never feel mentally fatigued; and at the other extreme there are the few highly psychasthenic persons who aver that they are seldom, if ever, free from the feelings of mental weariness. There are similar individual differences in fatigability as expressed by outward signs; the rapidly growing, the delicate, the dull, and the 'highly strung' are especially liable in their expression and output to show objective signs of mental fatigue. The obsessional type of psychoneurotic may be kept by his abnormally strong perseveration incessantly and perilously long at work, when the normal person would be unable to resist from taking protective rests. And not only the *·Mental breakdown'* obsessional, but even the mentally best balanced and most vigorous person, under conditions of sufficiently prolonged intense mental activity, will ultimately suffer, sometimes quite suddenly, from ·pathological' fatigue characterized by such wide-spread enduring disturbances that we describe the condition as one of ·mental breakdown'. We have not, however, any evidence that extreme muscular fatigue can ever cause such breakdown, although it may certainly conduce to ·physiological' mental fatigue. And when overwork is the prime cause of mental breakdown, it may well be that the psychoneurotic disorders that develop are due to the conscious or unconscious emotional disturbances induced *Emotional factors* or favoured by the collapse, through fatigue, of normal direction and control of them. Mental breakdown rarely appears to occur from mental overwork, and even when the latter is the only discoverable cause one suspects that an emotional factor has not been detected. The commonest cause of fatigue, using the term in the sense of a subjective complaint, is emotional conflict of some kind, ranging from some fairly clear-cut personal problem to the conflict associated with an on-coming psychosis. It might be said that mental fatigue arising from overwork alone is commonest in school children, less common in university students, and least common in an uncomplicated form in adults generally.

7.–SPINAL AND CORTICAL ANALOGIES

A little light is thrown not only on the pathology of ·mental breakdown' after excessive mental work but also on the manifestations of physiological mental fatigue, if we consider the effects of prolonged activity at

the lowest levels of the central nervous system. As the spinal flexion-reflex tires under continuous or frequent excitation it becomes weaker and more tremulous and may finally even cease altogether. But during this fading there occur brief periods of intermission and even of replacement by the antagonistic response of extension. Moreover, the flexion-reflex when tired is more easily interrupted than when it is fresh by the opposite extension-reflex, if simultaneously elicited. That is to say, under conditions of spinal 'fatigue' the suppression of antagonistic responses is no longer so effective; consequently, inhibited movements are more ready to break through.

*Analogous
mental case* Precisely the same occurs when we are at work in some particular field of mental activity. Antagonistic and irrelevant fields of attention are successfully inhibited, at first without voluntary effort owing to the affective incentive of interest but later, as spontaneous interests wane and boredom enters, through the exercise of volition. Finally as this 'directive' activity of the will fails through fatigue we can no longer, despite the utmost effort, attend to the work on which concentration is required; and ultimately we are unable to give continued attention to any field of mental activity. Thus local boredom gives place to general fatigue.

*Loss of
control* Such failure of control over antagonistic processes, accompanied by the tendency to 'spontaneous' excitement of what had been previously inhibited, must be recognized as one of the commonest phenomena of what is called mental fatigue. If we have already acquired a certain skill by the conquest of bad habits or, more generally, if we have in the past learnt to replace old associations by new ones, it is well recognized that in a state of mental fatigue those old habits or associations, no longer suppressed by inhibition, will once again make their appearance in place of the later ones. Thus mental fatigue will give rise to loss of skill, to failure of recent memory, and hence to accidents; and, especially in its pathological form, conflicts and complexes previously suppressed from consciousness will no longer be subject to the now fatigued higher inhibition.

Effect of rest A very brief period of rest proves sufficient for well-marked, although incomplete, recovery of the tired spinal reflex; its condition may therefore be reasonably attributed to a kind of synaptic 'block'. On the other hand, prolonged mental activity in a particular field of work causes more profound changes and needs for its restoration a longer period of rest or sleep; although, if it has not been too strenuous, a mere change of mental work, signifying perhaps relief from boredom, will suffice. Moreover, immediately after such rests or changes an initial loss of efficiency is inevitably incurred by the need once more to 'settle down' again to original working conditions—to 'get into our stride' again, as it were.

*Initial
facilitated
response* When we turn to the effects of continued or repeated stimulation of the flexor area in the cerebral cortex we find, as in the spinal flexion-reflex, that ultimately it fails to yield any response. But at first repeated cortical stimulation results in a facilitated increasing response, then in

a rise in sensitivity of the antagonistic extensor area, and finally in a quasi-epileptiform wave of movement, the stimulus spreading to neighbouring motor areas. Such facilitation of response has been found to occur initially in the mental fatigue associated with serious deprivation of sleep (M. Smith). It is perhaps analogous to that well-known release of normally inhibited 'reserve' activity which occurs in the initial stages of alcoholism. And it may be that the diffuse, no longer inhibited, responses which subsequently occur in repeated cortical stimulation are in some respects analogous to that collapse of the higher co-ordinating centres and to that wasteful dissipation and short-circuiting of energy characteristic of 'mental breakdown' through overwork, which variously manifest themselves in the inability to concentrate attention or to form decisions, in obsessions and anxieties, or in hyperaesthetic, hallucinatory, and other disturbances.

8.–GENERAL CONCLUSIONS

It is clear that mental fatigue is most evident and serious when the work *Fatigue of* is of a kind that demands prolonged concentration of attention and *'directive* that then its most prominent feature is a collapse of 'directive activity', *activity'* which manifests itself in impairment and distraction of attention, loss of skill, irritability, and other symptoms of loss of self-control, and finally in more serious disorders of volition, cognition, and emotion. But, in addition to such fatigue of volitional 'direction', we must also admit the likelihood of fatigue of the mental processes which are subject to such direction. At the one extreme we may recognize the fatigue of highly intellectual creative work, at the other the fatigue of such purely routine work as adding up columns of numbers. In both a certain direction and routine are inevitably involved, but in each their relative importance is clearly very different.

We must realize, then, that not only volitional 'direction' but also the *Of processes* processes which are subject to such direction must involve excitation, *subject to it* inhibition, and co-ordination. These several activities are, as we have seen, each liable to 'fatigue'. We have yet to learn the relations between the fatigue of directive activity and the fatigue of the processes which are subject to it. It is easy to suppose, if we assume their analogy respectively to a driver and his horses, that in fatigue of the former the horses escape from their driver's control; but it may also conceivably happen that they are themselves too tired at the time to run away. Hence, according to the balance between such opposing conditions, output may be initially increased in quantity or from the start diminished in quantity and quality.

On the physiological side we may conjecture that chemical bodies *Hypothesis of* adverse to excitation, inhibition, and co-ordination are formed, either, *biochemical* like acetylcholine, neurogenic or humoral in nature, or resembling in *cause* their action the toxins generated by excessive muscular activity. It may

also be that antitoxins resistant to such fatigue can be formed and that such drugs as caffeine act in this manner so as to dissipate or prevent fatigue. But we are as ignorant of these as we are ignorant of the supposed toxins and antitoxins responsible for, or defensive against, sleep. We are also ignorant of any differences which may exist between the fatigue caused by intensive or prolonged mental work and the fatigue caused merely by deprivation of sleep.

Therapeutic principles   Ignorant as we are of these different causes and kinds of mental 'fatigue', we can at present use only one common remedy—rest from work, at all events when the 'fatigue' is general, or at least change of work when the 'fatigue', as in early boredom, is due to waning of drives, interests, and other incentives—coupled, if necessary, with appropriate psycho-therapeutic measures when the fatigue is so serious as to be accompanied by psycho-neurotic disturbances. In all cases it is of first importance to ascertain what factors of a personal kind are contributing to the production of fatigue. In the majority it is these factors which are important rather than the overwork itself. Moreover, it must be remembered that habitual overwork is itself often the outcome of anxiety or of an anxious or obsessional temperament.

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FAVUS

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FEEBLE-MINDEDNESS

See MENTAL DEFICIENCY

FIBRILLATION, MUSCULAR

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Reference may also be made to the following titles:

1.–DEFINITION

488.] The name fibrillation, or fibrillary twitching, is given to momentary contractions of small bundles of muscle-fibres which occur spontaneously or in response to tapping, or to active or passive movement of a muscle. They may occur almost continuously in an affected muscle, first in one part and then in another, and may impart a flickering motion to the muscle and the overlying skin.

2.–DESCRIPTION

In fibrillation of such a flat and superficial muscle as the pectoralis major the skin over the fibrillating muscle fascicles is seen to be raised as though by very fine threads which run in the direction of the muscle-fibres. The mucous membrane of the fibrillating tongue may be 'on the work' almost as though it were a bag containing tiny wriggling worms, and as fibrillation of this organ is commonly associated with atrophy its shrunken and wrinkled appearance when fibrillating is very striking.

In healthy persons fibrillation of the orbicularis oculi (orbicularis palpebrarum) is a common phenomenon and may be powerful enough to move the upper lid in a quick 'wink' of slight amplitude. In fibrillation

of the large muscles of the limbs and trunk the muscle as a whole is not shortened and excursion of a limb does not take place, but in fibrillation of the thenar and hypothenar muscles little twitches of the digit may occur.

Fibrillation may be wide-spread both in association with organic nervous disease and in healthy persons. When not present in the resting *Evocation of* muscle, it may be evoked by passive stretching and shortening of the *fibrillation* muscle, as in the biceps by alternate flexion and extension of the arm, or it may follow relaxation after a powerful voluntary contraction of a muscle. Again, tapping will commonly elicit it in a muscle from which for the moment it is absent. Even exposure of the part containing the muscle to cold may elicit it.

Such a muscle commonly shows an increased myotatic irritability *Myotatic* (Gowers) when tapped, so that a visible local contraction of the part *irritability* tapped may occur. Thus in a biceps which is the subject of fibrillation (however caused), if the belly of the muscle is quickly pinched by the finger and thumb placed transversely across it, there will rapidly arise a transverse swelling across the belly which quivers for a second or two and then subsides, sometimes to be followed by wide-spread fibrillation of the muscle. Such a response is present in the healthy muscle but is notably increased in a muscle which is the seat of fibrillary twitching—for example in motor neurone disease.

Fibrillation affects muscle-bundles of different sizes; when large bundles *Fasciculation* of fibres are involved, the term fasciculation is sometimes used instead of fibrillation.

3.—AETIOLOGY

Fibrillation may be seen in normal persons, and if it occurs as an *In health* isolated sign, i.e. without muscular weakness, wasting, or other signs of nervous disease, has no untoward significance.

In tired or debilitated persons fibrillation of considerable extent and *In fatigue* persistence is common. It may be felt by the subject in the calves, thigh *or debility* muscles, glutei, or facial muscles, and may indeed be complained of as uncomfortable and exasperating.

It is in combination with wasting or weakness in the affected or *With* neighbouring muscles that fibrillation may express the presence of some *wasting* degenerative change in the motor neurone and thus have a serious import. In the progressive degeneration of the lower motor neurones known as progressive muscular atrophy (motor neurone disease) *Progressive* fibrillation is a striking and constant symptom, most evident when the *muscular* malady is rapidly advancing. It is present not only in the visibly *atrophy* wasting muscles but also in muscles not yet, but shortly to become, the seat of wasting. That is to say, in this malady the field of the musculature which shows fibrillation is larger than, and may be said to enclose, that which shows wasting. The twitchings are coarse (fasciculation), rapid, and continuous.

Degenerations of the lower motor neurones produced by compression, as in cord compression or syringomyelia, although they lead to wasting of muscles, do not produce fibrillation, or do so but inconstantly, feebly, and in limited extent. This is also true of the rapid muscular wasting which follows the acute necrosis of motor nerve-cells in poliomyelitis.

Neuritic type   Fibrillation is infrequent and minimal in the neuritic type of muscular atrophy (Charcot-Marie-Tooth, or peroneal type), and in the primary muscular dystrophies it is not seen at all.

It is not a common feature of the atrophic paralysis of multiple neuritis, or of single nerve lesions, but it may occur and persist indefinitely in the calf muscles after the subsidence of a severe sciatic neuritis.

Fibrillation does not occur, even when some wasting ensues, after lesions of the upper motor neurones, or in extra-pyramidal motor diseases, for example paralysis agitans.

Compression of nerve   Rarely, a slowly compressing lesion of a peripheral nerve or nerve-root may evoke twitchings of a fibrillary order in the muscles supplied by the nerve. Thus in cases of auditory-nerve tumour in which the facial nerve also is compressed facial twitchings may occur. A spinal-cord tumour may similarly affect the muscles supplied by a motor root pressed upon by the tumour.

In epilepsy   Coarser and more powerful muscle-fibre contractions, approaching in force and amplitude those known as myoclonus, and leading to movement of the muscle as a whole and sometimes of the part containing it, are occasionally seen in epileptic subjects. They may be of great frequency and persistence between the attacks.

4.–PATHOLOGY

Nothing is known of the changes in muscular activity and metabolism which lead to fibrillation, and the fact that free and extensive fibrillation may occur in a healthy person at times of fatigue or slight debility indicates that very great deviation from the normal need not be in question. It is not thought that the twitchings are due to active innervation of muscle-fibres, and this is probably also true in motor neurone disease.

5.–TREATMENT

In organic nervous diseases the treatment is that of the nervous affection. In healthy persons fibrillation rarely calls for treatment other than the general care and promotion of the subject's health.

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FIBROSITIS

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1.–DEFINITION

489.] Fibrositis is a non-suppurative inflammatory process affecting the white fibrous tissue; it may be relatively acute but is more commonly chronic. It may be limited to small areas, single or multiple, close together or sparsely scattered, or may affect a considerable area, such as the aponeurosis of the back or scalp or the panniculus adiposus. It is characterized by pain which may be acute and severe; it may be a dull aching with stiffness or complete inability to move the affected part— due to protective spasm in the early stages or to adhesions in more chronic cases. The wide distribution of white fibrous-tissue in the body leads to great diversity of symptoms depending on the other tissues affected. Fibrositis is the essential basis of muscular rheumatism and of many forms of neuritis, and the periarticular form may be confused with rheumatoid arthritis or with osteoarthritis, both of which conditions as well as gout are complicated by fibrositis in varying degree, as are many other morbid states.

2.–AETIOLOGY

Focal sepsis

Fibrositis is usually the result of the action of two or more aetiological factors. The most important is invasion by toxins which may be produced locally by small colonies of bacteria or may be derived from a distant source often in some part of the digestive tract, the tonsils, or the urogenital system (chronic urethral or prostatic infection). It may be associated with *Bacillus coli* infections; toxic absorption due to defective function in the colon is also a frequent cause of chronic fibrositis. The defect may be in the digestion of proteins which have not been reduced to the simpler amino-acids, or it may be carbohydrate indigestion of which oxaluria may be another indication. Normally such toxic matter is removed by the action of the liver. More acute manifestations occur in influenza, acute rheumatism, and gonorrhoea, and chronic fibrositis frequently accompanies both rheumatoid arthritis and osteo-arthritis.

Trauma

Bruising

Strains

Injury may also set up fibrositis but it is more likely to do this when the tissues are already affected by the action of toxins. Bruising with consequent effusion of blood and lymph may leave behind painful fibrous patches; sprains of muscles or ligaments may produce the same effect, for ligaments are so richly supplied with nerve endings that fibrositic changes in them may be very painful; hence the common use of the term neuritis for the condition. More important in the causation of fibrositis, however, are slight and repeated strains which may result from working in unnatural postures such as are incidental to many occupations. The overuse of untrained muscles causes stiffness; this familiar sequel to unaccustomed exercise soon disappears in the healthy, but more

persistent stiffness may result if the lymphatics and capillaries are un-
equal to the task of carrying away the products of catabolism. or if local
damage due to excessive wear and tear is. owing to defective circulation
or senile degenerative changes. not made good. Other examples of *Other causes*
fibrositis of traumatic origin are subacromial bursitis from strain on
the shoulder. tennis elbow, and Dupuytren's contraction which is often
due to chronic irritation of the palmar fascia: the holding of reins. a
tennis racquet. a walking stick, or certain tools may be the exciting
cause, though there is probably also a predisposing factor. The in-
cidence among Nottingham lace workers was once the subject of a
Home Office inquiry. Occupational fibrositis is more common in later
life when elimination becomes less efficient and repair less easy, and
merges into the fibrosis which characterizes senile degenerative processes.

Cold and wet, both climatic and local (e.g. exposure to draughts or a *Cold and wet*
wetting), have always been associated in the popular mind with chronic
rheumatism. Such causes act by depressing the circulation and dis-
ordering metabolism; the presence of toxic material from septic foci in
the system will increase the risk of fibrositis developing.

Gout may cause fibrositis. and there is reason to believe that this is *Gout*
more common than the articular form. It is associated with a high level
of uric acid in the blood which should be investigated; if the amount
exceeds 3·7 mgm. per 100 c.c. in men, or 3·5 mgm. in women, gout is
indicated, and specific treatment should be adopted.

Hereditary and constitutional factors are important. Thyroid deficiency *Heredity and*
leads to changes in the fibrous tissues and to deficient action of the *constitution*
sweat glands which may, though experimental evidence for this view is
lacking, render the elimination of toxins more difficult. Dupuytren's
contraction is often familial. Muscular rheumatism is not uncommon
in horses and in them there is a well-marked hereditary influence. certain
strains of race-horses being peculiarly liable to break down from this
cause during training as a result, not of errors in diet, but of slight
strains frequently repeated.

It is important to recognize the close relationship to other forms of *Relation to*
rheumatic disease and the analogy between fibrositis and arthritis. In *other*
the latter we have a wide range of pathological conditions ranging from *rheumatic*
                                                                        diseases
the acute infective type as met with in rheumatoid arthritis to the
traumatic and degenerative form. osteoarthritis. The question whether
rheumatoid and osteoarthritis are aspects of the same morbid process
or separate and distinct diseases is still debated. Similarly the question
arises whether such a form of fibrositis as acute lumbago or peri-
arthritis of the shoulder is an entirely different condition pathologically
from the stiffness of muscles and capsules of joints often met with in
advancing years; the former is probably due at least in some measure
to toxins of bacterial origin: another group of cases appears to be
caused by toxins of metabolic origin such as uric acid: and the senile
type may be compared to osteoarthritis, being due to trauma or wear
and tear associated with defective repair. The nodules met with in

fibrositis resemble in many respects those found in rheumatic fever and rheumatoid arthritis. though whether they are pathologically identical is a question calling for further research.

3.—MORBID ANATOMY AND BACTERIOLOGY

Inflammation Fibrositis may be due to the activities of many bacteria. The tissues may be infected by blood-borne bacteria, and the gonococcus is believed to act in this way; but it is more often due to toxins derived from distant foci which render the tissues more susceptible to the action of strains, chills, or other factors. The result is an inflammatory hyperplasia of the connective tissues usually in patches, with local exudation of serum and proliferation of fibroblasts; the walls of the small arterioles become thickened and nerve fibres may become involved in the exudate. The patches undergo resolution in favourable circumstances, but may persist and form local indurations or nodules varying in size from a grain of wheat to a bean, or may form strands causing adhesions between the muscles, ligaments, and adjacent structures. When fibrositis involves the joint capsules a form of fibrous ankylosis results from matting together of the folds of the capsular ligaments and adhesion to surrounding tissues. Bursae are often attacked and become adherent in the same way. Persistent nodules and indurations are liable to relapses and exacerbations, and thus enlarge to form large plaques which tend to contract like scar tissue. They are sensitive to meteorological conditions and dietetic indiscretions, becoming congested and painful.

Allergy Allergy has been invoked in this as in many other conditions to explain some aspects of the process, and the sudden onset characteristic of acute lumbago suggests such a cause. It is supposed that protein substances which have not been broken down into the simpler amino-acids by digestion enter the circulation, the intestinal epithelium which usually prevents their absorption failing in this respect in certain conditions. These proteins sensitize the tissue cells and the next time absorption of similar proteins occurs a reaction results and local areas of tissue necrosis are formed which may become the sites of nodule formation.

4.—CLINICAL PICTURE

(1)—General Symptomatology

Structures liable to be affected Pain and stiffness are the cardinal symptoms, varying in degree and with the part affected; minor symptoms will also depend largely upon the site. The principal structures liable to fibrositis are the superficial and deep fasciae, aponeuroses, ligaments and capsules of joints, tendons and tendon sheaths, bursae, periosteum, and the sheaths of the nerve trunks.

The onset may be sudden and acute with some fever, coated tongue,

scanty urine loaded with urates, and constipation. Acute lumbago is
the commonest form of acute fibrositis and sciatica may develop as a
result, but these conditions are dealt with elsewhere (see BACKACHE
AND LUMBAGO, Vol. II, p. 251, and SCIATICA). In the early and acute
stages pain may be so severe as to render any movement of the affected
parts impossible. and tenderness is often well-marked. Suitable treat-
ment generally gives prompt relief in the earlier attacks, but later
attacks may be more obstinate and tend to become chronic. Many
cases are insidious in onset and chronic from the outset; pain may then
be very slight and even absent during rest, stiffness being the most
notable feature.

Tension is an important cause of pain and is usually due to the swelling *Causes of*
of tissues where they are tightly bound down as in the case of muscles *pain*
lying between aponeuroses and bones. to strain upon inflamed liga-
ments, or to compression of nerves or nerve endings by the swollen
tissues as may occur where the roots emerge from the spine or in their
passage through the bony canals.

Careful palpation of the affected areas may reveal local indurations or *Nodules*
nodules which may be either quite superficial or deeply embedded in
or between the muscles; they may be exquisitely painful on pressure, or
may be entirely painless. They cannot always be detected and local
areas of muscular spasm due to defensive contraction to protect under-
lying inflamed areas may be mistaken for nodules. Application of soft
paraffin to the skin will make their detection easier. In chronic cases
they may not be tender unless a nerve fibre is involved in the exudate.
They are often more painful after rest and warmth in bed so that the
patient is stiff and aching when he awakes in the morning, these effects
wearing off gradually with exercise.

Stiffness varies widely in degree; there may be simply difficulty in *Stiffness*
performing certain movements, which can be overcome to a great
extent by effort; or movements in certain directions may be quite
impossible from the presence of adhesions. especially in periarticular
fibrositis. Permanent deformity may be the result.

Since the clinical picture depends largely upon the site of the fibrositis *Types of*
and the structures affected, the different varieties will call for considera- *fibrositis*
tion in some detail. Besides lumbago and sciatica to which reference
has already been made Dupuytren's contraction has been described
elsewhere (see DUPUYTREN'S CONTRACTION, Vol. IV, p. 272).

(2)—Panniculitis

Chronic fibrositis of the subcutaneous tissue or panniculus adiposus
is termed panniculitis. It is met with in its most characteristic forms *Sites*
where this type of tissue is accumulated, in the pectoral and mammary
regions, the loins and buttocks, to the inner side of and just below
the knee, on the flexor surface of the forearm, and in many other
places.

The skin becomes adherent to the subcutaneous tissues which are

thickened and denser than normal and, when an attempt is made to
pinch it up, dimples at the points of adhesion; the tissues are usually
somewhat tender on pressure but in the absence of pressure or tension
pain is usually absent. Fatty nodules are not infrequent in the affected
parts: they may be as big as a large bean but as a rule they are not
tender, which distinguishes them from the multiple neuromas of the
terminal cutaneous branches of sensory nerves. The clinical features of
panniculitis tend to merge into those of adiposis dolorosa (Dercum's
disease); but adiposity does not invariably accompany panniculitis.

(3)—Bursitis

*Types of
bursae*   Bursitis is a form of fibrositis which presents characteristic features.
Bursae vary in character from little more than an exaggeration of the
spaces of the areolar tissue associated with fatty pads, such as the bursa
beneath the insertion of the tendo Achillis, to definite sacs lined with
synovial membrane. The latter occur at the insertion of tendons in the
vicinity of joints with which they frequently communicate, synovial
effusion readily passing from one to the other, especially in the neigh-
bourhood of the knee joint.   .

*Clinical
picture*   Acute bursitis will be accompanied by considerable effusion and pain
from inflammation and distension of the sac, as may be well seen in
the prepatellar bursa in 'housemaid's knee', but where the effusion can
escape into a joint the pain may for this reason be less severe. In other
instances effusion is not prominent, but there is inflammation of the walls
of the sac as well as of the synovial lining, pain is apt to be severe, and
muscular spasm—a reflex defensive contraction which prevents move-

Adhesions   ment of the inflamed structures—is a characteristic feature. Adhesions
quickly form both within the bursa and to neighbouring structures,
which render movement painful, and thus cause much limitation and
crippling, for example in the subacromial bursa, or in the bursa at the
insertion of the obturator internus muscle into the femur where it may
give rise to one form of sciatica. The bursa between the outer aspect of
the great trochanter and the ilio-tibial band may become inflamed
from strain or injury; in this position, to a greater degree than in most,
melon-seed bodies may form, and the swelling may be so considerable
as even to suggest sarcoma.

As bursitis is so often associated with fibrositis of adjacent parts some
of the more characteristic symptoms will be described in dealing with
the shoulder (see p. 286).

(4)—Periarticular Fibrositis

*Diagnosis
from rheuma-
toid arthritis*   Fibrositis frequently affects the joint capsules and then closely re-
sembles rheumatoid arthritis; it begins, however, outside the joint and
does not involve the synovial membrane till the late stages, whereas in
rheumatoid arthritis the synovial membrane is the first point of attack
and, in the absence of effective treatment, results in disorganization of

the joint. This disorganization does not occur in periarticular fibrositis though there may be crippling from contraction of the capsule and consequent limitation of movement.

It may attack one joint only or many. Stiffness rather than pain is the *Distribution* conspicuous symptom and may be accompanied by crackling sounds *in body* on attempting movement after rest. The smaller joints are usually first affected and there may be some resemblance to Dupuytren's contraction but without the pronounced affection of the palmar fascia, though the tendons and their sheaths and the aponeuroses of adjacent muscles are liable to be implicated. It is chiefly met with in middle and later life and runs a very chronic course.

Dampness whether of climate, habitation, or occupation appears to *Causes* be a factor of importance in its causation but a history of vague attacks of rheumatism is often given. In view of the affinity of gonococcal toxins for the fibrous tissues it is possible that gonorrhoea may also be a cause. It may be a persistent sequel of subacute rheumatism or it may perhaps be more correct to say that its onset may have the characters of a sub-acute rheumatism.

Llewellyn described the condition in much detail but the most striking examples are found in French literature under the name, *'rhumatisme chronique fibreux'*. Knaggs described a form affecting the vertebral column under the name spondylitis ligamentosa.

Other differences from true rheumatoid arthritis are the absence of *Diagnosis* muscular wasting beyond that due to disuse, the absence of rarefaction *from rheumatoid* in the bones as seen in a radiograph, and the fact that the victims are *arthritis* often of a robust and healthy type as contrasted with the asthenic characteristics of the typical rheumatoid patient. It is not unusual for small osteophytes to form at the margin of the articular cartilage and at the junction of ligaments with bone from the tension of the contracted fibres, but the degenerative characters of osteoarthritis are absent except possibly in the very late stages.

In some recent classifications the condition is included in rheumatoid or focal arthritis and, as Llewellyn wrote, it belongs to the group of undifferentiated infective arthritides, but the course and prognosis, and in some respects the treatment differ, and therefore differential diagnosis is desirable.

(5)—Fibrositis of Head and Neck

Fibrositis of the occipital aponeurosis is a common cause of chronic *Fibrositis of* headache. Stiffness is not often noticeable, but tender nodules may be *occipital* detected, especially along the occipital ridge; the pain may be limited *aponeurosis* to the occiput or may extend to the frontal area: it is commonly worst in the morning and improves as the day goes on.

Neuritis of the seventh cranial nerve, Bell's palsy, is a form of fibrositis *Bell's palsy* affecting the sheath of the nerve in the aqueduct or in its passage through the foramen and is generally supposed to be due to chill, though the influence of a septic tooth or tonsil should not be overlooked (see

BELL'S PARALYSIS, Vol. II, p. 307). Other cranial nerves may be affected by fibrositis, but rarely.

Stiff neck   The neck and shoulder are often the seat of fibrositis; draughts are often regarded as responsible, especially in motor driving, but the wearing of heavy furs, sometimes more for decoration than warmth, may be responsible; they cause overheating, the wrap is thrown back, the heated and perspiring skin is exposed to the air, and fibrositis, which may be severe and acute but is more often chronic, follows. The weight of garments suspended from the shoulder is another possible cause. The ordinary stiff neck is usually due to fibrositis of the trapezius, and nodules may be detected in the edge of the muscle; the sternomastoids and other cervical muscles contract in order to protect the inflamed muscles and the familiar stiff neck results.

(6)—Brachialgia

Fibrositis of the shoulder is common and is generally acute, painful, and disabling; the shoulder joint from its mobility is very liable to strain and *Structures affected* this is an important aetiological factor. The structures most commonly affected are the subacromial bursa, the sheath of the biceps tendon, the tendinous intersections of the deltoid and, at a later stage as a result of extension of the process from the tissues mentioned, the sheaths of the nerve-trunks and the capsule of the shoulder joint.

Clinical picture   Injury is the most common cause but it may be associated with dental or tonsillar sepsis. The onset is often acute but sometimes the condition comes on slowly, and is then often associated with chronic trauma from working with the shoulder in a position of strain; knitting or similar work carried on for long stretches at a time is occasionally responsible for the milder cases. Pain may be very severe even at rest, and so-called brachial neuritis is due to this form of fibrositis.

Limitation of movement takes a characteristic form. The arm cannot be raised above the level of the shoulder and even this movement is performed by rotation of the scapula; if this is fixed, movements of abduction and internal rotation are usually impossible from spasm of the supra- and infra-spinatus and the teres minor. If the elbow is grasped and the weight taken off the structures around the shoulder joint, the head of the humerus can be rotated against the glenoid showing that the joint is unaffected.

Inflammation of subacromial bursa   Inflammation of the subacromial bursa is responsible for these symptoms; the bursa is a large sac with its roof formed by the acromion process and part of the deltoid muscle, and the floor by the tendon of the supraspinatus at its insertion. When the arm is abducted the bursa slides beneath the acromion and when inflamed will give rise to severe pain in doing so; in adduction there is a point, just below the tip of the acromion, which is very tender on pressure but, as the bursa passes beneath the bone in abduction, the tenderness disappears though the movement is usually too painful for this to be demonstrable. This has been called 'Dawbarn's sign'.

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In severe cases the inflammation spreads to the neighbouring structures *Spread of* and the axillary (circumflex) nerve, which winds round the neck of the *inflammation* humerus, may become involved: as a result of this there will be pain and hyperaesthesia in the area of its distribution and frequently also in the course of the radial (musculospiral) nerve which also arises from the posterior cord of the brachial plexus: pain is very commonly referred to the insertion of the deltoid. The acute condition tends to subside in a few weeks but, unless passive movements have been regularly carried out, a stiff shoulder due to resulting adhesions will remain and need to be moved forcibly under anaesthesia.

Synovitis of the sheath of the biceps tendon in the bicipital groove may *Synovitis of* give rise to similar symptoms though of less severity and the limitation *sheath of* of movement is usually limited to those actions which bring the biceps *biceps* into use. Pain is not very marked. Chronic strain is the usual cause and the onset is gradual. Tenderness will be most marked over the upper part of the groove.

(7)—Pectoral Fibrositis

Fibrositis of the pectoral muscles and the supporting tissues of the mammary glands is not uncommon. In addition to the causes already mentioned it may result from the weight and dragging of over-developed breasts. Although it does not differ in general character from that *Diagnosis* occurring elsewhere, it is important because it may suggest neoplasms *from new* or angina pectoris. It often appears to be aggravated by exertion such *angina* as a game of golf and then the suspicion of a cardiac origin is increased. *pectoris* Careful examination for local tenderness and nodules should make the nature of the disorder clear.

(8)—Intercostal Fibrositis

This condition, often called pleurodynia, may be erroneously regarded *Pleurodynia* as pleurisy, but any doubt should be removed by careful clinical examination. Diaphragmatic pleurisy on the other hand may be easily mistaken for fibrositis of the chest wall since pleuritic friction may not be heard in the early stage.

Fibrositis of the abdominal wall may give rise to suspicion of disease *Fibrositis of* of the underlying viscera, and laparotomy has sometimes been per- *abdominal wall and* formed in such cases. Fibrositis of the omentum has been described *omentum* but must be difficult to demonstrate.

(9)—Fibrositis of the Back

Fibrositis of the back and the gluteal regions is described under the titles BACKACHE AND LUMBAGO (see Vol. II, p. 251) and SCIATICA. Fibrositis of the ilio-tibial band may give rise to symptoms suggesting acute sciatica (see p. 284); it is more fully described under the title SCIATICA.

(10)—Fibrositis of the Plantar Fascia

uses   The plantar fascia may be the seat of a very chronic and painful fibrositis. It may be due to gonorrhoea and then affects the attachment of the fascia to the under surface of the os calcis where a nodule may form. and osteophytes are often revealed by X-ray examination. More commonly the condition is due to chronic strain thrown upon the muscles and fasciae of the sole by yielding of the plantar arch, to which attention must be directed.

(11)—Fibrositis in other Regions

Many bursae in the extremities may become inflamed but they do not call for separate description. One of the most important in this respect has already been mentioned, namely that beneath the tendo Achillis, and this form of bursitis which is generally the result of a strain is often very painful and disabling. Tennis elbow is discussed under the title ATHLETICS AND ATHLETIC INJURIES, Vol. II. p. 236.

The pain in all these conditions varies greatly: it may be continuous or intermittent, induced by movement, or, particularly in the chronic forms, by meteorological conditions, especially high winds, the onset of wet weather, damp, and fog. It may be very severe, sharp, and lancinating, or dull and aching; or it may be almost negligible, a sense of soreness or of general disinclination for effort, when the diagnosis will depend on the discovery of the typical tender spots or nodules which may only be detected after the most careful search.

5.–COURSE AND PROGNOSIS

The prognosis in fibrositis will depend upon the age of the patient, the parts affected, and the adoption of adequate treatment at an early stage. If time is wasted on homely remedies or quack nostrums adhesions will form and permanent stiffness may result. In early life fleeting attacks of 'muscular rheumatism' are common, but usually clear up without leaving any trace. Bursitis and periarticular fibrositis are not common until middle age or later and are much more likely to leave traces behind however thoroughly they have been treated. The malign forms, Dupuytren's contraction, and some cases of chronic articular fibrositis, pursue a steady and relentless course with gradually increasing deformity in spite of any treatment, but they are fortunately rare.

In all forms, however, fibrositic changes in later life tend to merge into degenerative fibrosis; the muscles are left stiff and slow in movement and the range of movement becomes less and less with successive attacks; this is especially seen in the hands of those engaged in arduous occupations, and in the bent back of senile kyphosis. The disease, though not mortal, may add seriously to the burden of advancing years.

6.—DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The principal features upon which diagnosis will depend have already been indicated in the discussion of the various forms of the disease: the mode of onset, the parts affected, and the presence of nodules are the most important. In connexion with acute cases it should be remembered that some acute infections, notably influenza, smallpox, and dengue, present muscular pains as a pronounced symptom. Pain and stiffness of the back may be due to ankylosing spondylitis, to meningitis, tuberculosis, syphilis, or tumour of the spine or the cord. Fracture of a vertebral body, especially of the type sometimes called Kümmell's disease, will give rise to symptoms which may be put down to rheumatism or intercostal neuralgia.

Herpes zoster before the appearance of the rash may suggest intercostal rheumatism, as the lesions may be very sparse and if on the back alone may be overlooked; in the aged an apparently mild attack may be followed by persistent pain but the accompanying hyperaesthesia should make the diagnosis clear. *Diagnosis from herpes zoster*

Paralysis agitans and the Parkinsonian syndrome which may follow epidemic encephalitis may cause doubt in those cases in which the rigidity of the muscles is more obvious than the tremor in the early stages; the facies often supplies a clue. *From paralysis agitans*

Dermatomyositis may easily be confused with fibrositis and can be distinguished by the presence of dermatitis, oedema, and progressive asthenia. *From dermatomyositis*

Trichiniasis is characterized by pain in the muscles which are swollen and show localized areas of tenderness. Oedema is usually present and the general course of the disease is such that fibrositis is not likely to be confused with it once it becomes well established; eosinophilia and leucocytosis will be present. *From trichiniasis*

Osteitis deformans may sometimes present pains in the back and limbs as a symptom. X-ray examination will reveal the characteristic appearances, and examination of the blood for increased phosphatase will aid the diagnosis. *From osteitis deformans*

The most serious problem in diagnosis is to distinguish disability due to fibrositis from hysteria or malingering, a difficulty that may often arise in workmen's compensation cases. Malingering is rare, but exaggeration is common. A man who feels that he presents little objective evidence to support his complaints is apt to overstate his case and it will be very difficult to determine exactly how much foundation there is for the symptoms of which he complains. Nodules must be searched for carefully; if they are not tender they are probably not important. If tender spots are troublesome, but nodules are not palpable, the areas should be marked and the examination repeated after an interval; it is improbable that the tenderness will be found in exactly the same situation on both occasions unless there is definite foundation *Diagnosis of malingering*

for it. Limitation of movement on account of the pain alleged to be caused by the attempt can only be disproved by careful watching; a patient with a stiff and painful back will appear quite unable to perform flexion and twisting movements when asked to do so, but may bend readily enough to pick up something from the floor when his attention is diverted from the examination. A useful test is to watch him when directed to turn over on the examination couch; it will often be seen that the spine is twisted in the attempt without any of the groans that accompany the movement when carried out to order. Contractures are often simulated and may be due to voluntary action or to hysteria, in the latter condition being maintained by muscle spasm which may persist for a long time or even permanently, as the result of secondary changes in the tissues due to shrinkage or adhesions. Such contractures may follow a genuine attack of rheumatic or traumatic origin, and the posture may have been adopted for the relief of pain in the first instance, pain of another kind developing later as a result of cramp in the muscle or persistent pressure on the articular cartilage. Suggestion may induce such a state or it may arise from a sense of grievance. It may be overcome by suggestion if the practitioner can convince the sufferer in a sympathetic manner that there is no organic foundation for his symptoms, whereas threatened or actual legal proceedings may simply fix it more firmly in his mind. Examination under an anaesthetic may prove that there is nothing seriously amiss, especially if it can be combined with suggestion while the patient is going under. Such conditions are quite as likely to be met with in robust individuals of fine physique as in those of weakly constitution, and in men as often as in women. A brusque and hectoring manner on the part of the medical examiner will do far more to intensify the trouble than to assist in diagnosis, the patient will be put constantly on his guard, and the chance of observing casual inconsistencies of movement and behaviour will be lost. (See also MALINGERING.)

7.–TREATMENT

(1)—General

The sooner thorough and effective treatment is adopted the better the prospect of regaining unimpaired activity. Too often the condition is regarded as trivial, a matter for household remedies or a 'rubbing bottle', and in consequence nodules become organized, adhesions are formed, and weeks of treatment are required to remedy the results of neglect.

In the acute forms of fibrositis it is essential to keep the parts at rest. If there is pyrexia, severe pain, or any marked constitutional disturbance, the patient should be kept in bed and on a light diet. In all cases of any severity and especially if the locomotor apparatus is affected, as in lumbago and sciatica, the duration of disability is likely to be lessened if this course is followed.

A brisk purge is generally advisable even if there is believed to be no **Purge** active constipation: calomel at bedtime followed by a saline in the morning is the most generally useful procedure, clearing the bowels of toxic material and stimulating the activity of the liver: this may be repeated two or three times with advantage. At this stage salicylates are useful in relieving pain and promoting the action of the skin: 20 grains of sodium salicylate with an equal quantity of sodium bicarbonate may be given every four hours if the fever and more acute symptoms have subsided. Aspirin in 15-grain doses four hourly may be preferred **Aspirin** and has a stronger analgesic effect; if tablets are used they should be crushed and taken with a good draught of water or gastric disturbance may be caused. In smaller doses aspirin may be continued after the patient begins to get about, but care must be taken not to produce diaphoresis if the patient is allowed out of doors. Cinchophen (phenyl- **Cinchophen** cinchoninic acid, atophan, agotan, phenoquin) and its derivatives (atophanyl, atoquinol, neocinchophen or tolysin) are useful in cases of metabolic origin and defective elimination which are generally due to gout, but must be given with due regard to their toxic action on the liver. These risks will be reduced if sodium or potassium bicarbonate is given at the same time: a tablet of 0·5 gram (7½ grains) may be taken with double the amount of the alkali in half a tumbler of water, or the alkali may be taken half an hour before a meal and the cinchophen after the meal, three times a day. Magnesium carbonate in doses of 5 or 10 grains is said to act better than the alkaline carbonates and to enhance the action of cinchophen, rendering smaller doses effective; it is therefore worth a trial. The administration of glucose also tends to protect the liver against the possible toxic action of the drug: in no circumstances should drugs of this type be used by the patient except under observation; they should not be taken for more than two or three days in succession and should be followed by an interval of equal or longer duration.

In the later stages and more chronic forms drugs are of little value. **Intestinal** Intestinal antiseptics may be of some service and of these salol is the **antiseptics** most generally useful; guaiacol carbonate is preferred by some and may be given with aspirin, 5 grains of each three times a day being a suitable dose. Another popular formula includes an allotropic form of iodine, **Iodine** namely, alphidine ½ grain with guaiacol carbonate 5 grains. Potassium iodide was formerly more popular than it is now in the treatment of rheumatic conditions, and has been supplanted by the organic forms of iodine and by various solutions, of which I prefer a saturated solution of iodine in 90 per cent alcohol (30 grains of iodine to 1 fluid ounce of rectified spirit), giving 1 minim in milk three times a day and increasing gradually to 5 minims or more. This may be given for four or five weeks and then an interval should be allowed. It is doubtful if these forms of iodine are as effective as potassium iodide; there is reason to believe that potassium as a base may be of some therapeutic value. Other forms of iodine, such as iodized oil (lipiodol), or iodolysin which also contains

tniosinamine, may be given intramuscularly with advantage in some cases.

Sulphur   Sulphur has for long been employed in the treatment of chronic conditions of fibrositic type as shown by the popular name of the confection of guaiacum and sulphur, 'Chelsea Pensioner'. The value of guaiacum is problematical, but sulphur has a laxative action and may influence the process of digestion in the intestine in other ways. How it acts after its absorption, if any takes place, is less obvious; it is claimed to be a catalyst and to promote the absorption of rheumatic thickenings. It is probable that onions and garlic, which as articles of diet are found to be useful by many rheumatic patients, act by reason of the sulphur

Garlic   compounds they contain. Preparations of garlic can now be obtained which do not to any great degree transmit to the breath the alliaceous odour which is the chief objection to these homely remedies. In one of these, allisatin, the garlic is combined with charcoal and is a useful remedy in chronic fibrositis. Injection of colloidal sulphur, of which there are several forms available, enables the sulphur to reach the tissues and at the same time to induce a mild artificial pyrexia; it is sometimes of service in cases in which there is a definite microbic or toxic factor. The colloidal form of sulphur may also be preferred for oral administration.

Thyroid   In cases of a metabolic type, especially when associated with obesity, panniculitis, or the menopause, thyroid is often of service. Half a grain of thyroid B.P. may be given three times a day and cautiously increased. Other endocrine preparations are of doubtful value.

Elimination of septic foci   A careful search should always be made for any septic focus from which bacteria or their toxins may be entering the circulation, and suitable treatment adopted. Teeth should be radiographed when their condition is doubtful; but a policy of wholesale extraction is rarely justified; not more than two or three at a time should be removed in view of the risk of flooding the system with toxins and of the shock entailed by more drastic procedures. Tonsillectomy should also be approached with caution and may be wisely regarded as almost a major operation in middle life or later, only to be undertaken if the indications are clear and urgent. Many cases of bursitis or 'neuritis' of the shoulder are caused by septic teeth; and similar infections of the tonsils, pharynx, or nasal sinuses are often found in cases of fibrositis of the neck, shoulders, or occiput. Septic conditions of the throat may be treated by painting the tonsils with Mandl's paint or organic silver preparations. Another useful method is to dissolve a pastille of colloidal iodine in the mouth three or four times a day; the iodine acts locally on the throat, and being absorbed may also exercise beneficial general effects.

Infection of prostate   Chronic non-specific infection of the prostate is far more common than is generally supposed and should be looked for and treated if present, especially in fibrositis of the back.

Cholecystitis and appendicitis   Cholecystitis and chronic appendicitis may be the cause of fibrositis but the relationship must be very obvious to justify surgical treatment.

Non-surgical drainage of the gall-bladder, however, may prove definitely useful and the following is a good method. Two drachms of magnesium sulphate dissolved in half an ounce of hot water are taken about two hours before breakfast, the patient then lies on his right side for half an hour when one or two cups of weak tea or hot water should be drunk; he may then rest a little longer before dressing. A copious evacuation of the bowel soon follows and a free discharge of the contents of the gall-bladder is associated with this effect.

The relationship of septic foci to rheumatic disease may be important even if there is not any direct association. A French physician has stressed this view by the remark that it is as important to deal with any such foci in proved gonorrhoeal rheumatism as in any other form, for the improvement of the general health and the raising of bodily resistance.

(2)—Vaccines

Vaccines have not proved to be of much service in the treatment of fibrositis, though when there is a definite focus of infection a trial may be justified. Since the patient will generally be already sensitized, small doses must be used. An obvious focus yielding a pure culture is usually *Autogenous* held to indicate an autogenous vaccine, but in most cases a mixed stock *or stock* vaccine will be more effective, acting as a non-specific desensitizing *vaccines* agent. An initial dose of a million of the mixed organisms should not be exceeded and some prefer to start with a tenth of this amount. As long as there is any reaction the dose should not be increased and if the reaction is at all marked it may be diminished to a half or less. In the absence of reaction the dose may be raised cautiously; an interval of four or five days should be allowed between the doses. A vaccine of intestinal bacteria is advocated by some though it is difficult to see on what grounds this is based; any effect it may produce is probably due to protein shock. A gonococcal vaccine may be tried when there is evidence of infection but is generally disappointing; the same technique should be followed.

(3)—Bee Venom and Protein Shock

Bee venom, originally advocated on the grounds that bee-keepers are not subject to rheumatism, has been used in the treatment of fibrositis with good results. Under various commercial names it is available in a form adapted for intradermal injection. A convenient form is 'apicur', *Administra-* the usual initial dose of which is 0·05 c.c.; it is administered by means *tion and* of a fine needle intradermally, i.e. into and not under the skin, an *dosage* essential point in the technique. Reaction is indicated by redness and swelling at the point of injection lasting one or two days, an increase in focal symptoms and possibly general effects, shivering, diuresis, and drowsiness. If the reaction is slight the next dose, given after an interval of three to five days, may be increased to 0·1 c.c., and subsequent doses may be 0·2, 0·3, and 0·4 c.c. or more if thought fit; it is convenient to

make separate injections for each tenth of a cubic centimetre. The active principle in the venom is believed to be related to snake venom, and not to formic acid as was formerly supposed. It has a non-specific protein effect and its use must be guided by the principles governing the use of other methods of this nature. Inquiry should be made as to any tendency to excessive anaphylactic reactions, such as asthma, urticaria, or hay fever, and when such a tendency exists the venom, if given at all, should be used in very small doses as unpleasant or even dangerous symptoms may ensue. The venom is supplied in different strengths and with different dosage according to the manufacturer, and attention must be paid to the special directions given.

The reactions vary considerably; in severe cases with much local swelling and general symptoms the dose should only be increased very gradually and the interval between the doses extended. A total of 1 to 1·5 c.c. constitutes a course and this may be repeated after three or four weeks. Amelioration of pain and stiffness will be experienced after four or five doses if the remedy is likely to be of service, and if this does not occur it is useless to continue. In some cases the symptoms tend to reappear some time after the treatment has ceased and the best results are obtained when physical treatment is given in addition.

Protein shock　　Protein shock may also be administered by the intravenous injection of typhoid-paratyphoid vaccine, the intravenous or intramuscular injection of peptone, or the intramuscular injection of sterile milk. Its effects are apt to be severe with the vaccine method and are too uncertain to be recommended in fibrositis in which better results can be obtained by other means. An exception to this may be allowed in the case of a combination of sterile milk with sulphur which is marketed under the name of pyrolactin D and gives mild reactions with possibly beneficial effects from the sulphur.

(4)—Physical Methods

Physical methods of treatment are of the greatest value in fibrositis, but in their use a clear conception of the condition of the tissues and the anatomy of the part is important, and the methods used must be adapted accordingly. Too often they are used in a haphazard manner because one or other happens to be at hand. Massage is 'tried' when it should be obvious that rest is required; elaborate procedures, electrical or otherwise, are adopted when simple homely measures would answer better.

Rest　　The necessity of rest in acute fibrositis has already been mentioned and in less acute conditions or localized forms it is often of equal import-
Strapping and plasters　　ance. In bursitis of the shoulder for example a sling should be worn to take the weight of the arm and should be so arranged as to pass over the opposite shoulder and not round the neck. Adhesive plaster on a good firm basis is of great service in securing rest in intercostal fibrositis and lumbago or sacro-iliac strain. The pain of tennis elbow may be relieved by a broad band of strapping just below the joint or by means

of a 'cock-up' splint. Strapping round the foot will often relieve painful conditions due to strain and consequent fibrositis of the plantar fascia and tarsal ligaments. A band of strapping an inch or an inch and a half wide is carried completely round the foot at the point where it will afford the maximum support to the affected ligament. 'Porous plasters' are a popular homely remedy and act largely by the support they give but also by keeping the part warm, an effect which is enhanced by the mild counter-irritation which is kept up. Belladonna or wintergreen plasters have a more marked effect on spasm and pain. While resting the part it is desirable to perform a full range of movements once or twice a day to prevent the formation of adhesions, especially in the case of the shoulder.

In the acute stages and for the relief of pain heat in one form or another *Heat* is of the greatest service. Vapour or hot-air baths may be given at home and inexpensive cabinets are sold for the purpose. Vapour baths are usually given at 110 to 120 F. for ten to twenty minutes. A much higher temperature can be tolerated with dry heat owing to the free perspiration and evaporation of the sweat from the surface of the body, and can be borne for a longer time.

Locally heat can be applied by means of poultices, hot compresses, or electric pads, and these methods are useful in fibrositis of the shoulder and back. For the extremities paraffin wax baths are used or the wax may be applied as a form of poultice. A wax of suitable melting point (115° to 120° F.) is heated in a double pan to about 130 or 140 F. and applied over the affected part with a large brush; it cools rapidly and five or six successive layers are similarly painted on; the part is then swathed in cotton-wool and left for three-quarters of an hour or so when the wax can easily be peeled off. Kaolin poultice may be used and kept on for as long as twenty-four hours.

One or more electric lamps in a suitable reflector provide a simple *Radiant heat* method for bringing an area under the influence of radiant or dry heat, and gentle massage can be carried on beneath the rays. Infra-red rays, which are said to be more penetrating, can be applied by various patterns of lamps made to be used with electricity, gas, or even paraffin. Diathermy may be used for deep-seated conditions, but does not present any advantages in most cases over the other means described. Heating treatments must not be carried to excess or they will do more harm than good.

Baths are valuable especially in the treatment of lumbago and *Baths* generalized rather than local forms of fibrositis. Taken at the outset they may ward off an attack entirely. From 102° to 105 F. is a generally useful range and higher temperatures may be used in the later baths for those who tolerate them well. During the bath, gentle rubbing of the affected parts and active or passive movements should be employed. Ten to fifteen minutes is a suitable duration, and drying should be carried out with a hot bath-towel. If perspiration is desirable, the patient should get into bed wrapped in the towel and be well covered with blankets.

Mustard baths

Baths may be modified by the addition of various substances. Mustard in the proportion of about a tablespoonful to every ten gallons has a well-established vogue as an addition to a bath. It should be made into a paste with cold water and then added to the bath. Such a bath is a rubefacient and is stimulating in proportion to the amount of mustard used. It is effective in general muscular rheumatism and in the stiffness following over-exertion or chill.

Brine baths

Brine baths may easily be given at home by the addition of one or two pounds or more of common salt or sea-salt to the bath of twenty gallons and in proportion for larger baths. They are stimulating and induce perspiration more freely than do plain baths, and a lower temperature may therefore be used.

Soda baths

Soda baths are often strikingly effective in relieving pain and stiffness in fibrositis, both acute and chronic. Common washing soda is used in the proportion of a pound to an ordinary bath. This strength may be increased, but it may have an irritating effect on the skin and will certainly damage the enamel of an ordinary bath.

Epsom salt baths

Epsom salts have a popular vogue and there is no doubt of their beneficial effect in some cases, although the reason for this is not obvious. The same strength and duration may be employed as for brine baths. Local baths may similarly be useful and may be stronger and of longer duration than full baths.

Massage

Massage is of great value especially in combination with the various forms of local treatment by heat. Discrimination is, however, necessary; it must not be used in the acute cases until active inflammation has subsided under the influence of heat and rest; this is especially the case in bursitis and fibrositis of nerve sheaths, and in other forms it may cause extension of the inflammatory process if begun too soon. At first only effleurage—gentle stroking and friction—will be tolerated and if necessary may be used with analgesic liniments, those containing methyl salicylate or substances of a similar nature being most useful. The counter-irritant liniments which have a popular vogue are not suitable at this stage but their stimulating effects answer a useful purpose in the more chronic forms. Gradually more vigorous treatment will be tolerated, firm rubbing and deep kneading directed to breaking down adhesions and dispersing nodules and indurations. Manipulation and passive movements may be necessary to restore full mobility, and forcible breaking down of adhesions under anaesthesia may be required if gentle movements have not been practised in the early stages. This applies particularly to the shoulder; the pain in the early stages causes spasm of the muscles around the joint and the rotation of the scapula may disguise the immobility of the joint. The arm whenever possible should be put through a full range of movements daily, slowly and gently; previous application of heat will make this easier.

Manipulation

Manipulation may be useful in some forms of fibrositis, but requires special knowledge if it is to be carried out successfully except in its simplest forms. After the more acute symptoms have subsided manipula-

tion directed to stretching the contracted ligaments and to overcoming muscle spasm may be carried out with advantage; gentle repeated movements will often succeed in this way without causing pain, and when the joint surfaces have been drawn apart and the muscle spasm overcome, passive movements may be carried out. (See also ATHLETICS AND ATHLETIC INJURIES. Vol. II. p. 229.)

Injection of procaine hydrochloride (novocain) has been advocated *Novocain* especially by French authorities. It is of special service in fibrositis around the shoulder joint and in the sacro-iliac region. The procedure is to inject 20 to 30 c.c. of a 0·5 per cent solution of novocain in physiological saline, infiltrating the whole of the painful area and thus inducing analgesia under which manipulations may be more easily carried out. Spasm may thus be overcome and permanent relief obtained. Minor displacements, which irregular practitioners so often profess to find, may actually be set up by muscle spasm and will be easily set right by this method. In sacro-iliac strain, injection of the ligaments has been advocated, but is difficult, and general infiltration will generally prove simpler and is often effective.

Ionization is often useful and may easily be employed in private *Ionization* practice without the need of costly and elaborate apparatus (see ELECTROTHERAPY, Vol. IV, p. 490). Suitable batteries for the purpose are supplied by manufacturers of electrical apparatus with the necessary electrodes made of sheet lead which can be bent easily to fit the part and bandaged in close contact. Various substances are used in dilute solution in which a pad of 12 to 16 thicknesses of gauze is soaked; this is applied to the painful part and the electrode fixed over it, with an indifferent electrode at a distance applied over a pad soaked in weak salt solution or placed in a bath for the hand or foot. Sodium salicylate is *Salicylate* useful applied in this way for the relief of pain: potassium iodide is used *Iodide* for the treatment of local thickening and induration; chlorine ions have *Chlorine* a similar action and for their production a preparation called T.C.P. may be advantageously used. All these substances are applied beneath the negative pole or kathode.

Another class of remedy is applied under the positive pole or anode. *Histamine* The most useful is histamine which sometimes gives very striking relief especially in the shoulder; it very quickly produces redness which goes on to an urticarial wheal, at which stage the application should cease. A material impregnated with histamine and known as katexon is supplied commercially and is the most convenient form for general use. With histamine the strength of the current and the duration must be determined by the reaction induced and will be influenced by the area of the electrode and the strength of the solution used; as little as 2 or 3 milliamperes for 2 to 5 minutes may suffice. With the other substances mentioned above a current of 40 to 60 milliamperes for 20 to 30 minutes is more generally useful.

Diathermy is often regarded as if it were a form of ionization since it *Diathermy* is applied in a similar way. Its action, however, is to generate heat in

the deeper tissues, and it is essentially a form of heat treatment like radiant heat and infra-red rays but acting more deeply. In my experience it is of less general utility; to obtain the best effect special skill and experience are essential, but often not available.

(5)—Spa Treatment

Spa treatment is perhaps the most effective of all measures in chronic fibrositis. The regime of rest and regulated mode of life with the skilled use of baths, massage, and douches will often clear up the most obstinate cases when all other methods have failed. The value of colonic lavage, which is a feature in many spas, is very great if used judiciously, and not only when constipation is a factor in the case. In fibrositis the external methods in use at spas are in most cases of more importance than the drinking of the water, and the choice of a spa will therefore depend to some extent on its equipment in this respect. The value of free elimination promoted by regular drinking of a suitable mineral water may, however, be considerable. At the same time it must be recognized that mineral waters differ from plain water, and also from

Saline waters each other, in their action on and through the skin. The strong saline waters like that of Droitwich are often very effective, as are also the

Sulphur waters bromo-iodine waters of Woodhall Spa. The sulphur waters are generally also saline though weaker, and their internal use enhances their external action; Harrogate and Llandrindod Wells furnish typical examples.

Thermal radio-active waters The thermal gaseous radio-active waters have for centuries enjoyed a reputation in the treatment of rheumatic conditions of all kinds and recent researches indicate that the gases pass through the skin and have an action in this way as well as purely externally; they are also eliminant through their diuretic action; examples are Bath and Buxton. At many spas packs of mud and peat are used and furnish an effective means of applying heat in conjunction with the specific action of the mineral water. The combination of douching and massage is widely used and is very effective in many cases, and a wide range of other methods of treatment is generally available. The general constitutional type of the patient must be considered in the selection of a spa, and the climate and general amenities will also influence the choice.

(6)—Diet

Diet is of importance but is not always at fault, and the most rigid dieting will not avail if there is an active septic focus, flat-foot or other

Restriction of carbohydrate postural strain, or if the disability is solely due to injury. There is some evidence that restriction of carbohydrates is helpful when there is a general tendency to fibrositis, as this may be associated with a high blood-sugar. Patients who are over-weight will also require food restric-

Idio-syncrasies tion especially in starches and sugars. An ample supply of uncooked fruit and vegetables is desirable, but some people get aches and pains after such articles as vinegar, acid wines, and some fruits. Others find that malt liquors are followed by similar symptoms and even by acute

lumbago. Inquiry must therefore be made for such idiosyncrasies in prescribing the dietary in fibrositis, even though no logical reason can be discovered for these effects. The value of onions has already been referred to. Ample supplies of fluids should always be taken. Alcohol in strict moderation does not appear to have any harmful effect in the absence of idiosyncrasy. In cases with a gouty tendency diet must be on lines appropriate to that disease.

(7)—Climate and Clothing

The combination of cold and wet is definitely unfavourable but not easy to avoid at some seasons in any part of Great Britain. Cold alone does not appear to have any unfavourable effect as judged by the records of Arctic expeditions. It is important to avoid damp houses, and the neighbourhood of large streams or collections of water. The sea is unfavourable in some cases but not all, and residence on higher ground a short distance inland is generally free from objection, open coast being generally preferable to a narrow estuary. The question of subsoil, clay or sand or gravel for example, is not entirely simple; a situation on a clay hillside with good subsoil drainage is preferable to sand or gravel in the bottom of a valley where the subsoil is likely to be water-logged. Thus the problem is complex and, unless the incidence of fibrositis is very high in the neighbourhood or there is other evidence that the climate is unfavourable to the patient, it is better to take steps to ensure the dryness of the house than to seek residence in some other place, where possibly conditions equally unfavourable in other respects may be met with.

Suitable attire is important for those with or liable to fibrositis, more *Clothing* so probably than in any other form of rheumatism. The idea that wool should be worn next to the skin has a wide popularity; and wool is certainly comforting to chilly individuals so long as it does not irritate the skin, since it is relatively non-conducting—a quality dependent in some degree on its closeness to the body and the possibility, desirable whatever form of clothing is worn, of circulation of air between the garments and the skin. This end is more readily attained by wearing porous or cellular materials, whether of linen or cotton, next the skin, with the outer clothing of woollen stuffs at least in cold seasons. Wool tends to absorb the perspiration and thus to keep a damp internal layer, and is also often dense in texture and prevents access of air to the skin. Silk has many advantages, but is too expensive to be available to many people: it is, however, noteworthy that a folded silk handkerchief worn next the skin over any affected part, for example the shoulder, often gives very marked relief. Briefly it may be said that clothes should be light and loose-fitting to permit of free ventilation and evaporation of perspiration while affording protection against the direct and local cooling effects of currents of air. There is no doubt that rheumatic troubles are more frequent in those who are too heavily clothed than in those whose wear is scanty, whose skins have retained a high capacity

for reacting to variations of temperature and thus protecting the body by natural means.

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FILARIASIS

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1.–DEFINITION AND CLASSIFICATION

490.] The name filariasis is applied to morbid conditions produced by nematode worms belonging to the family Filariidae (Cobbold, 1864),

Claus, 1885, examples of which belonging to various subfamilies are found in man as follows, according to Faust:

(i) Subfamily Filariinae Stiles, 1907. The representatives parasitic in man are *Wüchereria bancrofti* (Cobbold, 1887) and a subvariety now known as *Filaria malayi* (Brug, 1927). The former has until recently been known as *Filaria bancrofti*.

(ii) Subfamily Onchocercinae Leiper 1911. The representatives parasitic in man are *Onchocerca volvulus* (Leuckart, 1893) and *O. caecutiens* Brumpt, 1919.

(iii) Subfamily Loainae, Yorke and Maplestone 1926, of which the representative parasitic in man is *Loa loa* (Cobbold, 1864).

(iv) Subfamily Setariinae, Yorke and Maplestone 1926, of which the representatives parasitic in man are *Acanthocheilonema perstans* (Manson, 1891) and *Mansonella ozzardi* (Manson, 1897).

Of these various filariae only one causes any important pathological effects, namely, *Wüchereria bancrofti*, the adult forms of which live in the lymphatics and lymphatic glands and there produce various conditions due to lymph stasis. All these filariidae produce embryonic forms which inhabit the blood-stream or the connective tissues and possess a distinctive and recognizable morphology. For their transference from man to man an insect intermediary, usually a mosquito, is necessary.

2.–FILARIINAE

(1)—*Wüchereria bancrofti*

(a) Morphology

491.] *Wüchereria bancrofti*, formerly known as *Filaria bancrofti* (Bancroft), was renamed by Seurat in 1921 after O. Wücherer, its original discoverer.

Adult form　　The adult worms, white in colour, are long, transparent nematodes of cylindrical shape and with a smooth cuticle (see Fig. 56). Male and

(a)　　　　　(b)

Fig. 56.—*W. bancrofti* (natural size): (a) male; (b) female. (This and the following illustrations are from the Author's *Tropical Diseases*)

female are usually found coiled together and are difficult to separate *Male* from one another. The male is 40 mm. in length by 0·1 mm. in breadth. The tail is curved sharply ventrally and is furnished with two spicules of unequal length and an accessory piece. There are fifteen pairs of *Female* caudal papillae. The female measures 90 to 100 mm. in length by 0·24 to 0·3 mm. in breadth. The vulva is situated 0·6 to 1·3 mm. from the anterior end. The head is tapering and ends in a rounded swelling. The caudal extremity is narrow but abruptly rounded. The vagina,

0·25 mm. in length, leads into a uterus which soon divides into two branches. These uterine tubules coil back and forth throughout the *Embryos* greater part of the body, and are filled with embryos, or microfilariae, each of which is surrounded, as it lies coiled up, by a transparent oval membrane, which elongates eventually to form a sheath, encasing the embryo when it escapes from the vagina. The embryos escape in
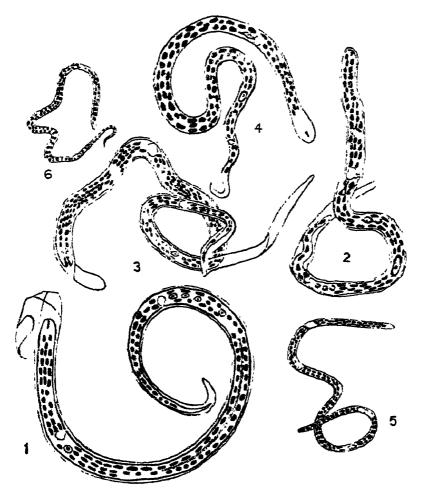
FIG. 57.—Microfilariae found in man: 1, Mf. bancrofti; 2, Mf. loa; 3, Mf. malayi; 4, Mf. volvulus; 5, Mf. perstans; 6, Mf. ozzardi. (Drawn to the same scale)

the active state, and the parent worms are usually described as being viviparous, but the condition is more accurately described as one of ovo-viviparity. The embryos, or microfilariae, on escaping from the gravid female, may either remain in the lymph or migrate through the lymph capillaries into the blood-stream.

The microfilariae are minute snake-like organisms measuring 130 to 320μ in length by 7·5 to 10μ in diameter and may occur in the blood-stream, lymph, and in the urine, as in chyluria (see Fig. 57).

It has, however, been noted that those in the lymph are shorter and thicker than those which have escaped into the blood and urine. In shape the embryo is bluntly rounded at its anterior end, but it is sharply attenuated posteriorly. Encased in its loosely enveloping sheath, the microfilaria moves gracefully, coiling and uncoiling itself when watched in a thick blood film, displacing in its snake-like movements clumps of red blood corpuscles. Directly the blood clot containing the embryos becomes cooled and the cells become consolidated, the embryos slip out of their sheaths and swim actively around in the plasma. In the unstained state few morphological details can be made out; in living worms the oral end is being constantly covered and uncovered by a
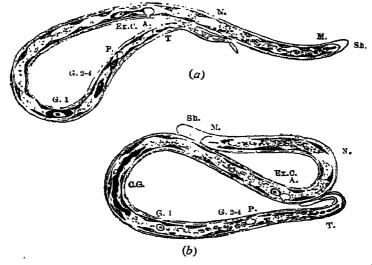
FIG. 58.—Minute anatomy of a microfilaria and differential points of structure between embryo of (a) L. loa and (b) W. bancrofti. N., Nerve ring; A., excretory pore; Ex. C., excretory cell; C.G., granular mass; G. 1-4, genital cells; P., anal pore; M., granules in mouth-cavity; T., granules in tail; Sh., sheath

prepuce, and from the uncovered end a delicate stylet is frequently protruded and then retracted. The object of this organ is possibly to enable a hold to be obtained upon the walls of the containing blood-vessels. When stained, the central axis of the microfilaria (see Fig. 58) is composed of a column of deeply staining nuclei. Other structures are a nerve ring (N.) in the anterior portion, an excretory pore (A.), an adjacent excretory cell (Ex. C.), and genital cells (G. 1-4) in the posterior part of the organism, three of the latter being grouped together in front of the anal pore (P.). The relative distances of these structures between each other along the long axis have been utilized in the morphological identification of these embryos, as they are constant in the same species.

(b) Periodicity

The microfilariae of W. bancrofti exhibit nocturnal periodicity, first observed by Manson in 1877. The term indicates that they are present

in the blood-stream in greater numbers during the night than during the daytime (see Fig. 59). In the variety of *W. bancrofti* which is found in the West Indies, India, and China this concentration of embryos in the peripheral blood takes place between 10 p.m. and 2 a.m., the numbers gradually increasing to the maximum at the latter hour; thereafter a gradual decrease takes place till 8 a.m. It has been calculated that as many as forty to fifty millions of these embryos are simultaneously circulating in the blood-vessels. This nocturnal periodicity is maintained with the utmost regularity—as long as twelve years in the case reported by Low, Manson-Bahr, and Walters. The microfilariae set free in the circulation live for at least fourteen days (Knott) and possibly as long
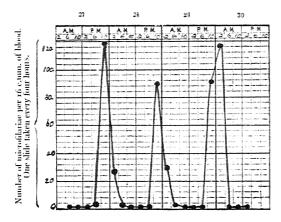
FIG. 59.—Filariasis (*W. bancrofti*, microfilaria nocturna) showing nocturnal periodicity

as ten weeks, as in the transfusion experiments performed by Hinman, Faust, and De Bakey.

A variety of *W. bancrofti* which is found in the Philippines (Ashburn and Craig), Tahiti, Fiji (Bahr), Samoa, and most of the islands of the central and southern Pacific Ocean is known as the non-periodic variety and is possibly a biological subspecies. In this form the embryos circulate in the peripheral blood as many by day as by night. This lack of periodicity does not bear any relation to the habits of the human host.

In the classical periodic *W. bancrofti*, as originally shown by S. Mackenzie and by P. Manson, the periodicity can be inverted by trans- *Inverted* posing the hours of sleeping and waking and, according to Yorke and *periodicity* Blacklock, a period of eleven days of inverted life is necessary for this to become established.

The underlying mechanism controlling periodicity has never been satisfactorily explained. My suggestion that it is a natural adaptation to the habits of the suitable insect intermediary host has obtained a certain amount of support from the fact that the non-periodic Pacific filaria corresponds in its distribution to that of its most suitable insect

Calcification of dead worms

FILARIASIS

intermediary in the regions where it occurs—*Aëdes variegatus*, which is a day-feeding species of mosquito, in addition to *Culex fatigans* which also acts as an intermediary.

(c) Development in Intermediary Host

In the appropriate mosquito (*Culex fatigans* in the case of the periodic *W. bancrofti* and *Aëdes variegatus* in the non-periodic form) the microfilariae pass into the stomach and in an hour or so become unsheathed (see Fig. 60). Passing through the stomach wall they enter the thoracic muscles in the course of the next twenty-four hours. Within two days they assume a sausage-shaped form, measuring 150μ in length by 10μ in diameter (see Fig. 61). Soon the internal nuclei multiply and become differentiated into alimentary organs, and within ten days to six weeks, depending upon the temperature and moisture, the larva elongates to a snake-like creature, 1·5 mm. in length, and migrates into the proboscis sheath.

FIG. 60.—Microfilariae casting their sheaths
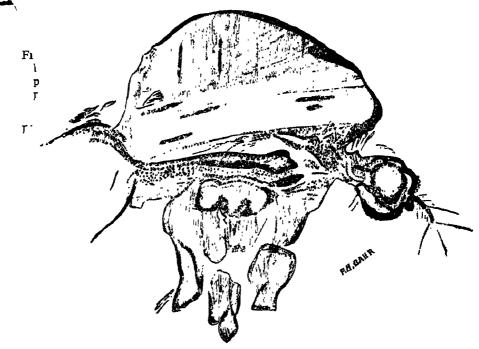
FIG. 61.—Section of thoracic muscles of *Aëdes variegatus*: second day after feeding on filariated patient

Eventually the larvae are extruded from the proboscis of the mosquito in the act of biting, and, by moving along the skin of the definitive host (man), they pierce through dermis and enter the body. The exact route by which they reach the lymph glands and the length of time required before the larval filaria attains maturity are alike unknown.

Complete development of *W. bancrofti* has been observed in the follow- *Mosquitoes* ing species of mosquito: *Culex fatigans*, *C. pipiens*, *Aëdes variegatus*, *acting as* *A. togoi*, *A. chemulpensis*, *Mansonia* *pseudotitillans*, *M. africanus*, *hosts* *Anopheles rossi*, *A. algeriensis*, *A. gambiae*, *A. ulceriensis*, *A. annictus*. *intermediary*

(d) Pathology and Morbid Anatomy

The chief pathological effects are produced by the adult *W. bancrofti*. Apparently in some cases these nematodes are able to exist in considerable numbers in the human body without producing any extensive disturbance of the lymphatic tissues, but usually some obstruction to the lymph flow takes place, and, whenever this is extensive enough to

Fig. 62.—Calcified *W. bancrofti* lying in and blocking a lymphatic vessel

interfere seriously with lymph function in spite of effective anastomotic channels, symptoms of filarial disease become apparent.

It was ascertained by Wise, and later by me, that after death the mature *Calcification* worms become calcified (see Fig. 62) and may be found in large numbers *of dead* (up to 200) in lymphatic vessels and glands scattered throughout the *worms* body, especially in the perirenal fat and pelvis of the kidney. In this calcified condition they continue to act as irritants and mechanically block the lymph channels. Giant-cell systems and fibrosis, especially of the lymphatic glands, form round the worms, while in the proximal lymphatic glands, in the afferent lymph-stream at some distance from the filaria worms, similar changes, accompanied by focal necrosis, take place. According to O'Connor the microfilariae are destroyed in the substance of the lymphatic glands in their efforts to pass through them and are also responsible for fibrotic changes. I have also shown that in this filariasis a further occlusion of lymphatic vessels by proliferation of the endothelium may occur (see Fig. 63).

(e) Clinical Picture

In many cases of infection with *W. bancrofti* manifest lesions or *Symptoms of* symptoms are not produced. In fact the greater the number of embryos *obstruction* in the peripheral blood, the fewer inconveniences the infected man appears to feel from their presence. It is only when damage to the lymphatic glands or lymphatic vessels has taken place that obstructive symptoms appear. These symptom-free cases are usually discovered

when a filarial survey is being undertaken, and it appears that in such hosts the adult worms may continue to discharge their embryos into the blood-stream for years without causing any inconvenience. It must, however, be borne in mind that the affected persons constitute a much greater danger to the community than do patients who show symptoms of disease and have fewer embryos circulating in the peripheral blood.

The pathological conditions produced by *W. bancrofti* are abscess-formation, lymphangitis, synovitis (especially of the hip-joint), varicose groin and axillary glands, lymph scrotum, orchitis, funiculitis, hydrocele, chylocele, chylous ascites, and elephantiasis. The condition known
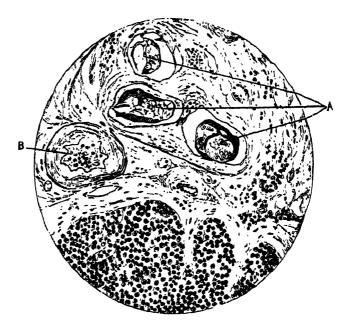
FIG. 63.—Section of a fibrosed lymphatic gland: A, portions of a calcified *W. bancrofti*; B, partially occluded lymphatic vessel

as filarial abdomen is due to pyogenic infection of the retroperitoneal lymphatics, leading to general peritonitis.

Abscess   Occasionally, when the parent worm dies and becomes infected with staphylococci or streptococci, an abscess results, in which fragments of the filaria may be found. The abscesses usually occur over the main lymphatic glands.

Lymphangitis   Lymphangitis is common in all forms of filarial disease and is associated especially with enlarged groin glands, filarial disease of the testis, spermatic cord, abdominal lymphatics, elephantiasis, and lymph scrotum. Painful cord-like swellings of the lymphatic trunks appearing like red congested streaks in the superjacent skin, and inflammation of the lymphatic glands, are visible at the beginning of the attack. This may last for several days and be accompanied by rigors, pyrexia, headache, vomiting, and sometimes delirium. The attack generally ends in profuse diaphoresis. The essential features of this form of filarial fever

have led to its confusion with malaria, especially in the West Indies. Some observers, notably Anderson, considered that an invading streptococcus was the cause of lymphangitis, but the most popular hypothesis at present is that it is an allergic manifestation of *W. bancrofti* infection. Usually within twenty-four hours of such an attack the microfilariae disappear from the peripheral blood. It may be that there exist two factors, septic and toxic, in lymphangitis. This view has been supported by the work of Lloyd and Chandra on complement fixation, extracts of *Dirofilaria immitis* being used as antigen. According to these workers there are two types of immunity response—a positive reaction associated with eosinophilia and a negative complement-fixation reaction associated with a polymorphonuclear leucocytosis.

Treatment of lymphangitis consists in elevating the affected part and applying cooling lotions and fomentations, and in the administration of mild aperients till the inflammation subsides. If lymph-containing vesicles should form, they should be pricked or scarified under aseptic conditions. *Treatment*

The concurrence of synovitis with other signs of filarial disease is common and may proceed to pus-formation with subsequent ankylosis. The knee is often affected, but in the Pacific islands it is the hip-joint which is most frequently attacked, necessitating surgical drainage of the joint, combined with removal of the inflamed iliac and inguinal glands draining the affected area. *Synovitis*

According to Rose and Grace treatment with a vaccine made from haemolytic streptococci is useful in mitigating attacks and preventing their recurrence. The initial dose should be 10 million organisms, increasing in doses of 10 million till the maximum of 50 million is reached.

The term varicose groin gland meant to Manson the soft doughy lymphatic swellings in the groins containing in their interior hard and enlarged lymphatic glands. They may involve one groin, or both, and are sometimes seen in the axilla. Varicose groin glands are often associated with other manifestations of filarial disease, such as hydrocele and lymph scrotum. These tumours should be differentiated from femoral herniae by the absence of a tympanitic note on percussion and by the failure to subside rapidly when the patient lies down. The difficulty arises when, as sometimes happens, they are associated with genuine hernia (see Fig. 64). *Varicose groin and axillary glands* *Diagnosis from hernia*

Unless they are associated with pain and recurrent attacks of lymphangitis, surgical interference with the object of removing these masses should be avoided. *Treatment*

The scrotum is enlarged and the skin is silky to the touch, with a large number of visible lymphatic varices which, when pinched, discharge large quantities of lymph or, occasionally, chyle. Microfilariae can usually be found in the discharging lymph as well as in the blood of the patient. This condition is usually a precursor of true elephantiasis of the scrotum. *Lymph scrotum*

Unless attacks of lymphangitis supervene or unless the disease is *Treatment*

tending to develop into true elephantiasis, lymph scrotum, if suspended and kept clean, is best left alone. If surgical treatment is necessary, the scrotum should be held down by an assistant and the testes pushed away. The diseased scrotum is cut away clear of the testes. Sufficient covering for the testes can be obtained by dissecting up the skin of the thighs. But if too much tissue is removed elephantiasis of the leg may supervene.

Orchitis, funiculitis and hydrocele   Recurrent attacks of orchitis, due to the presence of adult filariae in the tunica vaginalis and in the spermatic cord, lead to hydrocele and eventually may be associated with elephantiasis of the scrotum. In

FIG. 64.—Varicose groin glands in a Fijian with double hydrocele

orchitis the testis is at first enlarged and very tender, the epididymis subsequently becoming swollen, hard, and nodular.

Treatment   Treatment should be directed towards the relief of inflammation, and the hydroceles should be treated on ordinary surgical lines.

Chylocele   Chylous effusion into the tunica vaginalis is not uncommonly associated with lymph scrotum, varicose groin glands, and chyluria.

Chylous ascites   Chylous ascites, which is also associated with chyluria, is probably due to rupture of varicose chyle vessels into the peritoneal cavity.

Chyluria   Chyluria is due to the rupture of a lymphatic varix in the walls of some part of the urinary tract. Chyle then appears in the urine, and very often blood-cells (haematochyluria). Chylous urine looks like milk and con-

tains 1·8 to 2·6 per cent of fat, depending upon the amount ingested
with the diet, and almost invariably contains microfilariae. Chyluria
often appears without previous warning and is accompanied by pain
in the back and aching sensations about the pelvis and groins. Retention
of urine from the presence of lymphous clots sometimes occurs. This
manifestation is very likely to occur in women for the first time in
pregnancy or after parturition. It is curious that chyluria in *W. bancrofti*
infection occurs solely in association with periodic microfilaria, and not
with the non-periodic form. *Haematochyluria*

Lymphuria is the term applied to a similar condition in which the *Lymphuria*
abnormal element is lymph.

The treatment of chyluria should be conducted on symptomatic lines. *Treatment of chyluria*
The patient should be put to bed on an inclined plane with the feet
elevated, and treated by restricting the amount of fluid and by gentle
purgation and rest. Washing out the bladder with some bland solution,
such as boric acid, is the best form of active treatment to be adopted.
Recently O'Connor and Golden found improvement after X-ray irradia-
tion of the renal areas.

Filarial elephantiasis should be considered as the end result of filarial *Elephantiasis*
disease when the lymphatic channels are so blocked and choked with
adult filariae and their products that free lymphatic drainage is im-
possible. This is what Manson originally implied by the term hyper-
filariation. Doubts were formerly entertained on this subject because
of the frequent absence of microfilariae from the blood-stream in
elephantiasis. Many observers in India and China have recorded their
inability to find microfilariae in this condition. In my series of Fijian
cases of elephantiasis embryos were present in 38·2 per cent, and a higher
proportion than this, for reasons already expressed, could not be ex-
pected. Remains of defunct adult filariae have been demonstrated in the
midst of elephantoid tissue, and more recently O'Connor has demon-
strated that attacks of lymphangitis begin from 'focal spots' in the
blubbery tissue, and by X-ray examination has shown the presence
of dead and calcifying filariae in these areas.

In most cases (over 90 per cent) the lower extremities—either one or *Anatomical distribution*
both or in combination with the arms or scrotum—are elephantoid.
The scrotum is a favourite site for elephantiasis: the arms are more
rarely attacked, and still more rarely the mammae, vulva, and limited
areas of the limbs or trunk. The disease usually begins with lymphangitis
or cellulitis, accompanied by pyrexia (usually known as elephantoid
fever), and the lymphatic glands draining the affected area are enlarged
and tender. The affected parts soon increase in size, the surface of
the skin becomes rough and coarse, the hair becomes rough and sparse,
and the nails are thickened and deformed. There is usually not any
distinct line of demarcation between the healthy and the diseased skin.

Elephantiasis of the legs usually does not spread above the knee, and *Treatment of elephantiasis of the legs*
the swellings may attain enormous dimensions and involve the whole
extremity, so that in aggravated cases the legs may attain a circumference

of several feet. The patient should at first persevere with elastic bandaging, massage, and elevation of the limb. Elastic stockings are uncomfortably hot and may be painful; in order to avoid this they may be made to lace up at the sides. It is most necessary to protect the affected limbs against injury. Various operative measures, none entirely satisfactory, have been devised. Kondoléon's operation consists in the incision of the fascia lata and removal of large sections of the aponeurosis with the idea that removal of this tissue assists in the anastomosis of lymph channels and veins.

Kondoléon's operation

Auchincloss's operation

Auchincloss's operation aims at removing those tender 'focal spots' whence the inflammation arises. It consists of two incisions marking out a vertical strip of skin, from the ends of which V-shaped incisions are made diverging upwards at the upper end and downwards at the lower.

Elephantiasis of the arms

Elephantiasis of the arms is comparatively common in association with the non-periodic Pacific *W. bancrofti* but rare elsewhere. It is secondary to mass infection of the epitrochlear lymphatic glands by adult filariae. These glands become grossly enlarged and fibrosed and are precursors of the elephantoid condition. Surgical treatment has been attempted on the same lines as described above.

FIG. 65.—Elephantiasis of scrotum; left leg slightly affected

Elephantiasis of the scrotum

Scrotal tumours may attain an enormous size (see Fig. 65); some weighing 10 to 20 pounds are by no means uncommon, the largest recorded weight being 224 pounds.

Treatment

This is the form of elephantiasis most benefited by operative treatment. If the tumour is of considerable size, the patient should be kept in bed for at least a week before operative measures are undertaken.

Operation

Spinal anaesthesia, reinforced with gas and oxygen, is the most suitable. With the patient in the lithotomy position, the scrotum should be drawn down and elastic webbing applied so as to expel the blood, a short rubber cord being wound round the neck of the tumour and firmly secured. A vertical incision is made down to the penis so as to free this organ, for usually the skin of the glans penis is normal. At this juncture a urethral sound should be passed so as to prevent injury to the urethra. The vertical

incision should be continued round the scrotum as far as the perineum, and the scrotum should be divided into two halves. The testes and spermatic cords are separated from the blubbery tissue, the hypertrophied gubernacula being divided. At the base of each half of the scrotum clamps are fixed, care being taken that these are situated well to the proximal side of all diseased tissues. Each half of the scrotum is then cut away through healthy tissue. Every visible blood-vessel must be securely tied and the clamps gradually loosened. The skin in the upper and inner aspects of the thigh is undermined and brought together over the testicles. Skin grafts may have to be applied to the penis at some later date.

Elephantiasis of the vulva and of the mammary glands is rare, but the breasts or the labia majora, if inconveniently large, may have to be removed. Instances have been recorded in which an elephantoid mammary gland has weighed as much as 21 pounds after removal. Tumours of the labia may weigh 10 pounds or more.

Elephantiasis of vulva and mammary glands

(f) *Diagnosis*

The diagnosis of filarial infections is made most readily by the demonstration of the appropriate microfilariae in the blood. When, however, the embryos are absent, auxiliary methods must be employed. Serological and intradermal tests have been introduced by Fairley (1931), and by Taliaferro and Hoffman.

The antigen is made from the heart worm of the dog, *Dirofilaria immitis*, from which, when dried, an alcoholic extract is obtained. For the intradermal test 0·25 c.c. of a 0·1 per cent extract is used; an immediate as well as a delayed reaction is obtained, a wheal 2 cm. in diameter being considered positive. The test is on the whole more useful for the diagnosis of *Loa loa* infections than for *W. bancrofti*.

Intradermal test

(2)—*Filaria malayi*

The microfilaria alone of *Filaria malayi* (Brug, 1927) is known, obtained originally by Lichtenstein from natives of Celebes (see Fig. 57). It was studied by Brug, who found that it differed in minor points from the common microfilaria of *W. bancrofti*. There are no nuclei in the anterior 12 to 16μ of the worm. From the region of the anal pore the body decreases to a sharp caudal extremity where there is an elongated nucleus, and about 10μ in front of this there is a deeply staining oval nucleus. Development takes place in the mosquitoes *Mansonioides annulipes*, *M. annulatus*, *M. uniformis*, *M. annulifera*, and *Anopheles sinensis*.

The distribution of this filaria, as at present known, is Java, Sumatra, and other islands of the Malay Archipelago, and it has not spread further east than the Moluccas and the Lesser Sunda Islands. It also has a patchy distribution in Ceylon.

3.—ONCHOCERCINAE

(1)—*Onchocerca volvulus*

492.] *Onchocerca volvulus* (Leuckart, 1893) inhabits the subcutaneous tissues, forming tumours, especially in the intercostal spaces, axilla, popliteal space, and suboccipital region. It is found along the west coast of Africa from Sierra Leone to the Congo, where in Belgian territory 68 per cent of the natives are affected.

Morphology   The male is 20 to 40 mm. in length by 0·2 mm. in breadth. The tail terminates in a single spiral and is bulbous at the tip. The female is 60 to 70 cm. in length by 0·4 mm. in breadth. The head is truncated and round. *O. volvulus* is ovo-viviparous. The egg possesses a peculiarly striated shell and has a pointed process at each pole. At least four males and two females are present in every tumour. The embryo or microfilaria is sheathless and measures 300μ in length by 8μ in breadth. The body tapers and ends in a sharply pointed recurved tail.

Although found in the fluid of the tumour cavity, the parasites may occur in the skin of widely separated portions of the body, even in apparently healthy natives. The embryos are ingested by the buffalo gnat, *Simulium damnosum*, in the thoracic muscles of which they undergo a development similar to that of *W. bancrofti*.

Clinical picture   *O. volvulus* forms tumours of various sizes from that of a pea to that of a pigeon's egg, which in the incipient stages may give rise to considerable pain. They have been found in children of two months of age and in elderly people may form the starting points of neoplasms. Lymphatic enlargement of the scrotum with hydroceles and enlarged testes has been noted by Laigret, and localized abscess formation has been noted by Chesterman (personal communication).

Skin changes   Lichenoid eruption of the skin, or a dermatitis, is often associated with *O. volvulus* infections, especially in Europeans, and in South American cases in the variety known as *O. caecutiens* (see below). Associated with these skin changes the patient experiences terrible pruritus, especially *Diagnosis*   at night. The diagnosis is made by snipping off a piece of skin near an onchocerca nodule and placing it for 15 minutes at 37° C. in saline solution; the microfilariae escape from the tissues and can be seen in centrifuged preparations.

Treatment   Treatment of onchocerciasis consists in excision of the tumours, especially when they give rise to pain, although usually in the African form they appear to be painless.

(2)—*Onchocerca caecutiens*

O. caecutiens Brumpt, 1919 is the South American form, first found by Robles in 1919. It is now known to occur in 95 per cent of the population of the Pacific slopes of Guatemala between 1,800 and 6,000 feet. In Mexico de la Torre has seen over 15,000 cases. There are not any certain morphological distinctions between *O. caecutiens* and *O. volvulus*.

Development takes place in *Simulium avidum*, *S. ochraceum*, and *S. mooseri*, and it is said that over 11 per cent of caught wild flies contain developmental forms of *O. caecutiens*. This is popularly known as the 'blinding filaria', so called on account of its association with punctate keratitis and the predilection of the tumours to form on the head. Robles has described epileptiform convulsions due to perforation of the cranium by tumours of the periosteum. In the eye the microfilariae are found in the choroid and posterior two-thirds of the cornea, and as they are phototropic they can be seen by the corneal microscope (see p. 221). Their presence easily accounts for the pathological lesions observed.
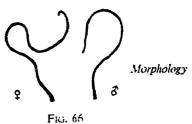
Treatment of this form of onchocerciasis also consists in the removal *Treatment* of the operable tumours, and is said to improve the eye conditions considerably.

4.–LOAINAE

493.] *Loa loa* (Cobbold, 1864) is widely distributed in West Africa, from *Distribution* Sierra Leone to Benguella, and follows the course of the Congo and its tributaries to a point about 1,500 miles from the mouth. *L. loa* inhabits the subcutaneous and connective tissues and often crosses the conjunctiva of the eye.

The male measures 30 to 34 mm. in length, *Morphology* with a breadth of 0·4 mm.; the cuticle is embossed with protuberances. The female varies from 20 to 70 mm. in length, with a breadth of 0·5 mm. (see Fig. 66). The embryo, or microfilaria diurna, is very similar in size to

Fig. 66
Loa loa (natural size)

that of *W. bancrofti* but differs in possessing a tougher sheath, in its irregular outline when dried, and in possessing characteristic large and deeply staining 'genital cells'.

The periodicity of this microfilaria is exactly the reverse of that of *Periodicity* microfilaria bancrofti, for the embryos disappear from the peripheral blood at night and swarm in the middle of the day. The periodicity is therefore diurnal and cannot be reversed, at least with the same ease as in microfilaria bancrofti.

Development of the microfilaria outside the human body takes place *Development* in the mangrove flies, *Chrysops dimidiata* and *C. silacea*. The larval forms are found in the thoracic muscles and the 'fat body' of the thorax and head. Full development takes about ten days, after which the larvae are found in large numbers in the insect's proboscis. It would appear that after the larva has entered the human body, development to full maturity is not attained for several years.

As a rule the symptoms of this parasite do not give rise to serious incon- *Pathogenicity* veniences, except when it crosses the eye. Fugitive swellings, known as *and symptoms* 'Calabar swellings', often occur in natives and Europeans in West Africa (see Fig. 67). These swellings, which are usually situated on the arms or

legs, may appear on any part of the body and are generally about the
size of a goose's egg. They usually last about three days, but sometimes
they may persist for several weeks, especially when situated on the face.
On the hand or forearm they give rise to a sensation of soreness, as if
the part had received a severe blow. As a rule they are hot both sub-
jectively and objectively. Disappearing as mysteriously as they have
arisen, they are now regarded as allergic reactions of the tissues in
response to the toxins given off by the parasite (F. Fülleborn; and N. H.
Fairley).

Treatment   No specific treatment has been discovered for this filarial infection.
Cool compresses and cooling lotions appease the pain, and heliobrom
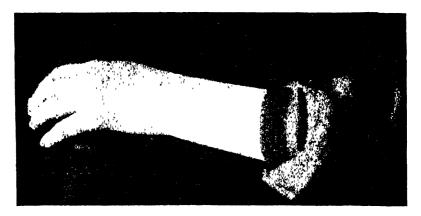
FIG. 67.—Calabar swelling on dorsum of hand in European lady
from the Congo

(described by the makers as dibromotannate of urea) 10 per cent in 70
per cent alcohol relieves the irritation. Other lesions produced by the
filaria are urticaria, dermatitis, hydrocele, abscess formation, and lymph-
atic oedema of one or both legs.

5.–SETARIINAE

(1)—*Acanthocheilonema perstans*

Geographical   494.] *Acanthocheilonema perstans* (Manson, 1891; Railliet, Henry, and
distribution   Langeron, 1912) is very common throughout tropical Africa, especially
on the West Coast and in Northern Rhodesia and Uganda. It has been
reported from western Venezuela, Trinidad, the Guianas, and northern
Argentina. It is possibly also abundant in New Guinea. This filaria does
not produce any pathological effects as far as is known.

Morphology   *A. perstans* is a long cylindrical filaria. The male measures 45 mm. in
length by 0·06 mm. in breadth; the tail is incurved. The female measures
70 to 80 mm. in length by 0·12 mm. in breadth. The adult worms are
found in the mesentery, perirenal and retroperitoneal tissues, and peri-
cardium. The embryo, or microfilaria, is sheathless and observes no

periodicity (see Fig. 57). It is found mainly in the big blood-vessels and measures 200μ in length by 4·5μ in breadth. It tapers acutely towards the tail. Development takes place in small midges, *Culicoides austeni* and *C. grahami* in the Cameroons, and probably in species allied to this genus in other parts of the world. **Intermediary hosts**

(2)—*Mansonella ozzardi*

Mansonella ozzardi (Manson, 1897; Faust, 1930) is found in the New World and appears to have a peculiarly restricted distribution. It has been found in the Carib Indians of British Guiana, St. Vincent and other West Indian Islands, and also in the northern provinces of the Argentine. The adult forms have been rarely found in the mesentery and visceral fat.

The male is 32 mm. long by 0·2 mm. in breadth; the female 65 to 81mm. in length by 0·25 mm. in breadth. The microfilariae measure 173 to 240μ in length by 4 to 5μ in breadth. They are unsheathed and non-periodic. The caudal extremity is sharply pointed (see Fig. 57). **Morphology**

Development is similar to that of *A. perstans* and takes place in a midge, *Culicoides furens*. As far as is known, *M. ozzardi* has no pathogenic action. **Intermediary host**

6.–MICROFILARIA STREPTOCERCA

495.] Microfilaria streptocerca (Macfie and Corson, 1922; Stiles and Hassall, 1926)—only the embryonic form being known—was first described by Macfie and Corson in biopsy of the skin, especially in the cutis and corium, of natives of the Gold Coast. More recently it has been found widely distributed in the Cameroons. In the first series no less than 44 per cent of subjects, who were otherwise in good health, were found infected. **Distribution**

The microfilariae are sheathless, tapering anteriorly and posteriorly with a transversely striated cuticle. They range from 180 to 240μ in length by 3μ in breadth. The anterior end is rounded, and the tail extremity is incurved like the handle of a walking-stick. Sharp has shown that in vital staining its capacity for dyes is slight, like that of *W. bancrofti*, as contrasted with the strong affinity of the microfilariae of *O. volvulus*, *L. loa*, and *A. perstans*, and that development does *not* take place in *Simulium damnosum*. **Morphology**

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FINGERS

FISSURE AND FISTULA
OF ANUS

See ANUS DISEASES, Vol. I, p. 645

FITS

See CONVULSIONS IN INFANCY AND CHILDHOOD, Vol. III,
p. 406; *and* EPILEPSY, p. 96

FLEAS

See ARTHROPODS AND DISEASE, Vol. II, p. 120; CHIGOE DISEASE,
Vol. III, p. 116; *and* SKIN AFFECTIONS DUE TO
INSECTS AND ACARINES

FLIES

See ARTHROPODS AND DISEASE, Vol. II, p. 120; BITES AND
STINGS, Vol. II, p. 343; *and* SKIN AFFECTIONS DUE TO
INSECTS AND ACARINES

FLUKE INFECTIONS, INTESTINAL

SECTIONS 1 AND 3 TO 7

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Reference may also be made to the following titles:

BILHARZIASIS   CLONORCHIASIS   LIVER DISEASES

                  PARAGONIMIASIS

1.—FLUKES

496.] The flukes or Trematoda belong to the phylum Platyhelminthes (flat worms). They have flattened oval bodies and may vary from 0·1 mm. to almost 7 cm. in length. One or more suckers may be present, anterior or ventral in position: the latter are prehensile, the former *Alimentary* alimentary in function. The alimentary canal consists of a mouth *system* situated in the oral sucker, a muscular pharynx which may be absent, and a thin-walled oesophagus which divides posteriorly into two blind intestinal caeca. Food consists of blood, cells, and the semi-digested intestinal contents of the host.

The nervous system consists of two large supra-oesophageal ganglia *Nervous* joined by a transverse commissure. From these nerves pass out to *system* other organs.

The main excretory ducts enter the excretory sac in the middle line; *Excretory* this sac discharges by the excretory pore. *system*

The genital organs are for the most part hermaphrodite; both sets, *Genital* male and female, open by a common genital pore. The yolk glands are *system* much branched, and a shell gland is also present. The uterus contains many ova; passing down the oviduct these are fertilized by spermatozoa from the receptaculum seminis. Into this organ they find their way in the process of cross-fertilization; auto-fecundation can occur. Often the receptaculum communicates with the exterior by Laurer's canal, which in some species acts as a vagina and serves for the entrance of spermatozoa in copulation. The fertilized egg receives yolk from the vitelline glands and a chitinous shell from the shell gland. When completed, the ovum, having entered the uterus, passes to the exterior.

The life cycle of the Trematoda is a sexual generation alternating with a parthenogenetic generation, the germinal cells of the sporocyst being ova developing parthenogenetically.

There are two life cycles: (i) in the Monogenea—development into a *Life cycle:* non-ciliated larva which changes directly into a sexual hermaphroditic *Monogenea* animal; and (ii) in the Digenea—development into a ciliated larva which *Digenea*

enters into molluscs, leeches, or fishes, encysts, and takes on a second larval form. The egg consists of a cell surrounded by yolk granules. The shell is oval and often provided with an operculum. When laid, the egg generally contains a ciliated miracidium, which swims actively about in water and can develop further on entering an intermediary host, generally a freshwater snail, in the liver or digestive organ of which it becomes a sporocyst containing numbers of germinal cells. Agglomerations of these cells may give rise to (i) cercariae, larval trematodes provided with one or more suckers and a tail which serves for progression; (ii) daughter sporocysts; and (iii) rediae, provided with an oral sucker and a rudimentary intestine. In these rediae further cercariae are produced; moreover, the germinal cells inside the original redia may give rise to daughter rediae.

In some species the cercariae are set free from the snail and make their way into the water, in which they can live for about forty-eight hours. In some instances they shed their tails and pierce the skin of their definitive host, and in others, as adolescercariae or metacercariae, they encyst in another animal, plant, or fish, and are taken in by the definitive host in food or drink. In the definitive host the immature flukes migrate to their site of election—the liver, the lung, the intestinal canal, or in some instances the blood-stream.

FIG. 68.—*Fasciolopsis buskii*: ventral view (life size). After Odhner, *Centralblatt f. Bacteriologie u. Parasitenkunde*, 1902

2.–FASCIOLOPSIASIS

(1)—Morphology

497.] *Fasciolopsis buskii* (Lankester, 1857) Odhner, 1902 are pinkish in the fresh state and vary from 2 to 7 cm. in length by 0·5 to 2 cm. in breadth, being about 2 mm. in thickness (see Fig. 68). Normally they are an elongated oval, slightly narrower anteriorly than posteriorly, and differ from *Fasciola hepatica* in not having a cephalic cone. The cuticle is covered with spines. The oral sucker looks forwards from the anterior end and is about 0·5 mm. in diameter; the ventral sucker, or acetabulum, lies a short distance from the anterior end and measures 2 to 3 mm. in diameter. The genital pore opens immediately in front of the acetabulum.

The intestinal system is composed of a very short prepharynx, a small muscular pharynx, and a very short oesophagus, which divides into the two unbranched caeca in front of the ventral sucker. The testes are large branched glands placed one behind the other in the posterior half of the body and between the caeca; vasa efferentia run forwards from the testes and enter the large cirrus pouch where they dilate to form two seminal vesicles before uniting to enter the cirrus. The oötype and

shell gland form a globular structure occupying almost the exact centre of the worm, and the branched ovary lies on its right; there is no receptaculum seminis. The uterus pursues a convoluted course anteriorly, beginning just in front of the female genitalia and ending within the genital atrium. The vitelline glands consist of very numerous follicles occupying the fields external to the caeca from the level of the acetabulum to the posterior extremity, where the two vitellaria meet to form a continuous band round the posterior border (see Fig. 68).
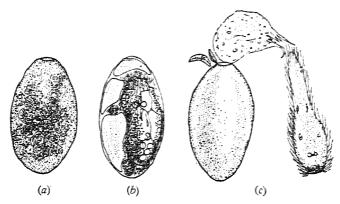
FIG. 69.—Eggs of *Fasciolopsis buskii*. (*a*) Immature egg from faeces; (*b*) egg with mature miracidium; (*c*) miracidium escaping from egg shell. × 200. (After Barlow, *American Journal of Hygiene*, 1925)

The eggs are oval with a clear thin shell and an operculum at one end. *Eggs* They measure 130 to 140μ in length by 80 to 85μ in breadth (see Fig. 69). When passed in the faeces they are immature and must remain in water for two weeks or longer, depending on the temperature, before the miracidia attain maturity and escape.

(2)—Life Cycle

A schematic representation of the life cycle is given in Fig. 70. The *Miracidia* miracidia can live for 6 to 60 hours free in water according to the temperature, after which they die unless they make contact with a suit- *Snail hosts* able snail, i.e. different species of planorbis: *P. coenosus*, *P. schmackeri*, *P. largillierti*, and *P. nitidella*. According to Ishii the excretion of the cephalic glands dissolves a cone-shaped hollow in the shell of the snail, forming a 'penetration-ring', to the edge of which the small parasite gains attachment and is thereby enabled to enter the snail more deeply. The miracidia enter the lymph spaces of the snail and form sporocysts in which the mother rediae appear in 14 days; the daughter rediae escape from the mother rediae in 25 days and in 30 days contain mature cercariae which finally escape from the snail in 31 to 35 *Cercariae* days. These times are taken from Ishii and apparently apply to a temperature of 28° C., and they differ widely from the times given by other workers, who were probably using different temperatures.

When the cercariae escape from the snail they swim actively for only a short time, which is all that is needed, for they encyst on the plants on which the snails are feeding. The most important plants are the water calthrops, *Trapa natans* in China and *Trapa bicornis* in India, and the water chestnut, *Eliocharis tuberosa*, in parts of China and Formosa. The natives of the various countries eat the fruits of these plants in the raw state and as a preliminary they tear off the corms with their teeth, thus affording an opportunity to the cercariae encysted thereon to enter the mouth. The cercariae are next swallowed and, passing through the
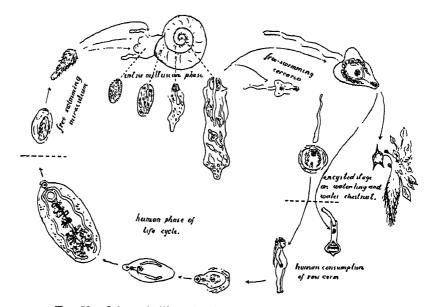
Fig. 70.—Schematic life cycle of *Fasciolopsis buskii*. (After Faust)

stomach, excyst in the duodenum, in which they immediately attach themselves to the mucous membrane and grow to adults.

*Geographical
distribution*
Fasciolopsiasis has been recorded in various localities in all the countries between central China and Bengal on the mainland as well as in many of the East Indian islands, especially Formosa. It is probable that this region may be eventually extended, for recently several obviously indigenous cases have been found in a village in Bihar, north-west of Bengal.

*Definitive
hosts*
Man and the pig are the common definitive hosts, although the presence of the infection in these two does not coincide in all places. The dog has also been found naturally infected in Canton.

(3)—Pathology and Morbid Anatomy

The worms live attached to the mucous membrane and cause inflammation and erosion with round-celled infiltration and perhaps a *Sites of
attachment* certain amount of haemorrhage. Their usual sites of attachment are the duodenum and upper part of the small intestine, but they have been found everywhere from the stomach to the ascending colon. A heavy

Infection may suddenly cause intestinal obstruction. There may or may *Blood picture*
not be leucocytosis, but there is always a great increase in eosinophils.
The red cells may be slightly reduced in number, but severe anaemia
is not a prominent feature except towards the end of a heavy infection.

(4)—Clinical Picture, Course and Prognosis

Symptoms do not arise until about three months after infection. In
light infections there may be nothing more than occasional slight
epigastric pain; in heavier and well-established infections the pain often
resembles that of a duodenal ulcer, being relieved by taking food.
Diarrhoea comes on early, and there may be five or six pale offensive *Diarrhoea*
stools in the twenty-four hours, and these attacks may alternate with
periods of constipation. After the infection has lasted for some months,
the diarrhoea becomes worse, and the patient begins to show signs of
anaemia. Oedema now appears and involves the face, abdominal wall, *Oedema and*
genitalia, and the lower limbs, and there is also ascites which causes *ascites*
prominence of the abdomen, especially in children. It is stated that fluid
is not found in the pleural cavity except in cases of great severity and
fatal termination. The appetite remains good, although there may be
nausea and vomiting. At a late stage the skin becomes harsh and dry
and is a dirty yellow. Finally, death may occur from exhaustion brought
on by the continuous diarrhoea and aggravated by the toxaemia and
the renal and cardiac conditions that follow on the generalized anasarca.

Recovery is rapid after the worms have been eradicated, so that if a *Prognosis*
case is treated before the late complications have set in the prognosis is
good.

(5)—Diagnosis

This rests upon the detection of eggs in the stools. They are difficult *Eggs in*
to distinguish from those of *Fasciola hepatica*, but the latter infection *stools*
is extremely rare in the countries where *Fasciolopsis buskii* is endemic.
The gravity flotation methods for concentration of nematode eggs in
stools are of no use in demonstrating the eggs of this parasite.

(6)—Treatment

Human infection could generally be prevented if the various water *Prophylaxis*
nuts known to carry the infection on their corms were dipped in boiling
water for a few seconds to kill the encysted cercariae before removing
the coverings.
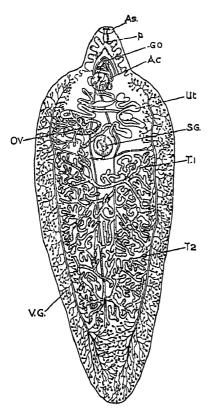
Most of the drugs used for eradicating hookworms are successful *Betanaphthol*
in fasciolopsiasis. Betanaphthol may be given in three doses each of
25 grains at intervals of half an hour for adults; for children a reduced
dose is used depending on the age and physical condition of the patient.
Carbon tetrachloride in doses of 3 c.c. for adults is also valuable, but *Carbon*
it must be administered with care on account of its toxicity, especially *tetrachloride*
in alcoholics. From my small experience tetrachlorethylene appears *Tetrachlor-*
just as efficacious and is preferable because of its relative non-toxicity; *ethylene*

it can be given to adults in daily doses of 3 to 4 c.c., and in proportionally smaller doses to children. Oil of chenopodium is not suitable.

3.–FASCIOLIASIS

498.] *Fasciola hepatica* Linnaeus, 1758, is a large fluke which has a wide distribution. It is a parasite of many herbivores, such as the ox, sheep, goat, camel, llama, elephant, horse, donkey, rabbit, guinea-pig, squirrel, antelope, and roe-deer. The kangaroo, monkey, and occasionally man are also infected. Normally it lives in the biliary passages of its mammalian host and produces a disease known as 'liver-rot'.

FIG. 71.—*Fasciola hepatica* (× 4)

As., anterior sucker; Ac., acetabulum or ventral sucker; P., pharynx; G.O., genital opening; Ut., uterus; V.G., vitelline glands; OV., ovary; S.G., shell gland; T.1 and T.2, testes. Posterior branching of intestine is not shown. (Partly after Sommer in Brumpt's *Précis de parasitologie*)

(1)—Morphology

Fasciola hepatica is 30 mm. in length by 13 mm. in breadth. It is flat and leaf-like. At the anterior end there is a conical projection, and posteriorly it tapers bluntly. The integument is provided with spines. There are two suckers. The acetabulum is conspicuous and is situated near the base of the cephalic cone and measures 1·6 mm. in diameter, the oral sucker being considerably smaller. The anatomy is very similar to that of *Fasciolopsis buskii*. (See Figs. 68 and 71.)

The species found in domesticated animals in the tropics is *F. gigantica*. Pigulewsky reported nine human cases of infection with this worm from Tashkent.

(2)—Life Cycle

The eggs are light brown in colour and measure from 130 to 145μ in length by 70 to 90μ in breadth.

Development of the contained embryo takes place after oviposition. The eggs, which are deposited in the biliary tracts, pass into the intestine and out with the faeces.

The developmental cycle of *F. hepatica* is the classical example of the life history of a fluke and takes place outside the human body in fresh-

water snails of the genus *Limnaea*, as first demonstrated by Leuckart and Thomas. The most efficient intermediary in Europe is *Limnaea truncatula*. Other appropriate species have been recorded from other countries. The miracidium, after escaping from the egg in water, *Miracidia* undergoes metamorphosis into a sporocyst in the digestive organ of the mollusc. These sporocysts migrate into the intrahepatic lymph spaces *Sporocysts* and produce rediae, which in turn may either produce other rediae *Rediae* parthenogenetically or give rise to cercariae; the latter, on erupting *Cercariae* from the snail, swim about in the water and encyst eventually as minute spheroid objects on meadow and swamp grasses and plants. When these grasses are eaten (and with them the cercariae) by mammals, the larvae (adolescercariae) excyst in the duodenum and penetrate the gut-wall to reach the peritoneum, whence they pierce the liver through Glisson's capsule and wander about in the liver substance, causing considerable destruction of tissue. Not until they have almost attained sexual maturity do they penetrate the bile-ducts where they lay their eggs.

(3)—Pathology and Morbid Anatomy

Cases of fascioliasis hepatica in man are very rare. One of the commonest sources of infection is water-cress. The presence of these flukes in the biliary passages causes cystic dilatation and eventually fibrosis of the ducts. There is a gradual replacement of the liver cells by scar *Hepatic* tissue, resulting in pressure atrophy of the portal vessels. Eventually *cirrhosis* complete cirrhosis takes place with ascites.

Human infections have been recorded from Venezuela, Cuba, Argentina, France, Russia, Hungary, Greece, Egypt, and China.

In some cases *F. hepatica* has been found in the blood-vessels, lungs, ventricles of the brain, and the circumorbital tissues.

In the Lebanon district of Syria a curious form of human infec- *'Halzoun'* tion is said to be not uncommon. This disease is colloquially known as 'halzoun' and consists of the attachment of adult flukes (*F. hepatica*) to the pharynx, when they have been ingested in the raw livers of sheep and goats which have been 'sacrificed'.

This localized infection produces local symptoms, such as oedema of the soft palate, pharynx, larynx, and even the nasal fossae and Eustachian tubes; very rarely asphyxiation may ensue.

(4)—Diagnosis

Diagnosis is made by the recognition of the eggs of *F. hepatica* in the faeces. The infection necessarily has to be distinguished from that produced by *Fasciolopsis buskii*, as the eggs resemble each other closely. According to Khouri the eggs may be recognized in the bile obtained by the duodenal sound.

(5)—Treatment

As far as experience in human cases has gone, it tends to show that *Filix mas* liquid extract of male fern, *Filix mas*, given in the same manner as for

tapeworms, is most efficient in expelling these flukes (see TAPEWORM INFECTIONS, INTESTINAL). Lièvre (1934) reported favourably on a dye, 'Magdala rose', injected intravenously in a 1 per cent solution. This substance is excreted exclusively in the bile and is an excellent fasciolicide. Khouri and his collaborators in Cuba maintain that emetine is specific for this infection when given intramuscularly. The average total dose is 3·72 mgm. of emetine hydrochloride per kilo body-weight, spread over a series of five infections.

'Magdala rose'

Emetine

Jeremy and Jones reported a cure with carbon tetrachloride, 2·4 c.c. being given on three occasions with fourteen days' interval between the doses. Carbon tetrachloride in 1 c.c. doses is the standard remedy for fluke infection in sheep. Occasionally it causes fatalities, and cattle are so susceptible that it is not recommended for them.

Carbon tetrachloride

4.—OPISTHORCHIS FELINEUS

Morphology

499.] *Opisthorchis felineus* (Rivolta, 1884), a lanceolate fluke, is closely allied to *Clonorchis* and measures 8 to 11 mm. in length by 1·5 to 2 mm. in breadth. The cuticle is smooth and the suckers are of equal size, separated from each other by one-fourth of the body length. The eggs are small and yellowish-brown, 30μ in length by 12μ in breadth. The normal hosts of the species are the dog, cat, glutton, and pig; but it is found quite commonly in man in East Prussia, Siberia, Annam, and the Philippines. The cysts derived from infected fish have been found by Vogel to pass through the stomach unaffected but to be freed in the small intestine. Attracted by the bile the young flukes travel up the bile-duct into the liver within five hours of being swallowed. Maturity is reached within four months.

Life cycle

The development of the parasite outside the body takes place in a freshwater snail, *Bithynia leachi*, and the ripe cercariae, measuring 0·34 mm. by 0·24 mm. encyst in freshwater fish such as bream, tench, chub, carp, and barbel. This species does not appear to be specially pathogenic to man, although 200 or more have been found in the liver and bile-ducts at autopsy.

5.—HETEROPHYES HETEROPHYES

(1)—Morphology

500.] *Heterophyes heterophyes* (v. Siebold, 1852), Stiles and Hassall 1900, is a minute fluke which occurs as a natural infection in the cat, dog, fox, and man. It is found in Egypt and the subtropical countries of the Far East. It is an elongated pyriform fluke with a broadly rounded posterior and is pointed anteriorly. It measures 1 to 1·7 mm. in length by 0·3 to 0·4 mm. in breadth. The spines covering the body are close to one another and more numerous at the anterior than

Morphology

towards the posterior part of the body. The ventral sucker is thick-walled and situated at the junction of the first and second thirds of the body. There is a characteristic horseshoe pad, bearing spines, around the genital pore, the oral sucker being much smaller. The alimentary canal consists of a long prepharynx, which leads into a bulbous pharynx, succeeded by an oesophagus which bifurcates to form the intestinal canal. The excretory bladder is terminally situated. There are two oval testes situated at the posterior end of the intestinal caeca. The ovary is situated in the middle line near the anterior margin of the posterior third of the body. The oötype lies transversely and is surrounded by small shell glands, and the uterus opens under the male opening in the genital pore (see Fig. 72). The eggs are operculate and light brown in colour. They measure 28 to 30 by 15 to 17μ.

FIG. 72.—*Heterophes heterophyes.* A, greatly magnified; B, natural size; *m.*, mouth; *p.b.*, pharyngeal bulb; *oes.*, oesophagus; *i.*, intestine; *ut.*, uterus; *v.g.*, vitelline gland; *r.s.*, receptaculum seminis; *ac.*, acetabulum or ventral sucker; *g.r.*, genital ring; *g.p.*, genital pore; *ov.*, ovary; *L.c.*, Laurer's canal; *t.*, testis; *ex.p.*, excretory pore

(2)—Life Cycle

The egg, hatching in water, gives rise to a miracidium which develops in the freshwater molluscs, *Melanoides tuberculatus*, *Cleopatra bulimnoides*, and a conical snail, *Pirenella conica*. The cercaria is oculate and has a lophocercous tail and was formerly known as *Cercaria lophocerca* (Sonsino). The metacercaria is found in freshwater fish, such as the mullet, *Mugil cephalus*, and a minnow, *Gambusia affinis*. The encysted adolescercaria is coiled upon itself. When liberated from the cyst capsule it bears a resemblance to the adult fluke, and infection of the mammalian host is effected by consumption of the raw flesh of the fish. Although the mullet is normally a freshwater fish it enters the sea to spawn. The infected fish are usually caught in brackish water.

(3)—Pathology

These flukes bury themselves between the folds of the mucous membrane of the small intestine, to which they are attached by their suckers. There are usually large numbers of eosinophil cells and leucocytes in the mucous membrane, but marked pathological changes do not occur. In cases of heavy infection digestive disturbances may result, and even diarrhoea may develop.

(4)—Diagnosis

Diagnosis is made by the detection of the characteristic eggs, and sometimes the adult worms, in the faeces. The eggs are ovoid, thick-shelled, and operculate. In colour they are pale yellow.

(5)—Treatment

There is good evidence that in course of time most of the heterophyid trematodes become detached and are spontaneously evacuated. Thymol in full doses (60 grains), betanaphthol (10 grains), and carbon tetrachloride (60 minims), these doses being for adults, all act as anthelmintics in this infection. The administration of magnesium sulphate in one-ounce doses removes large numbers.

6.–METAGONIMUS YOKOGAWAI

501.] *Metagonimus yokogawai* Katsurada, 1912 (*Synonym—Loxotrema ovatum*, Kobayashi 1912), a small fluke which was first described as *Heterophyes yokogawai*, is the commonest species of heterophyid fluke in China and the Far East, as well as in many of the Balkan States. The adult fluke lives attached to the intestinal mucosa of man, the dog, the pig, and the pelican (*Pelicanus onocrotalus*).

Hosts
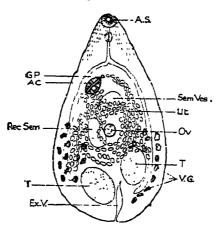
FIG. 73.—*Metagonimus yokogawai* (× 45). A.S., anterior sucker; G.P., genital pore; A.C., acetabulum or ventral sucker; Rec.Sem., receptaculum seminis; T., testis; Sem.Ves., seminal vesicle; Ut., uterus; Ov., ovary; V.G., vitelline glands; Ex.V., excretory vesicle. (Partly after Leiper)

(1)—Morphology

It is pyriform in shape and measures only 1 to 2·5 mm. in length by 0·4 to 0·75 mm. in breadth. The body is provided with integumentary scales. The ventral sucker, or acetabulum, lies to the right of the middle line with its long axis directed diagonally. The oral sucker is small and leads into a short prepharynx, and then into a globose pharynx and oesophagus, which gives rise to a pair of intestinal caeca.

The two testes lie in the posterior part of the body; the vasa efferentia, going to form the vas deferens, expand into a seminal vesicle. The ovary is a globular body situated in the middle plane at the posterior half of the body and is apt to be mistaken for a ventral sucker. The vitellaria, or yolk glands, are arranged in a fan-like distribution in the lateral aspects of the worm (see Fig. 73).

The eggs are light yellowish-brown operculate oval structures, measur- *Eggs*
ing 26·5 to 28*μ* in length by 15·5 to 17*μ* in transverse diameter and can
be differentiated only with great difficulty from those of *Heterophyes
heterophyes* (see p. 329).

(2)—Life Cycle

The first intermediary snail hosts of this fluke are *Melania libertina*, *First inter-*
M. ebenina, or allied species. First sporocysts, then mother rediae and *mediary hosts*
daughter rediae are formed. The cercariae of the fourth asexual generation
which emerge are characteristic. They have an oblong body, attenuated
anteriorly, and a long lophocercous tail. The body is provided with
spines, and in the anterior third there is a pair of pigmented eyespots.
The extreme anterior end of this cercaria, like that of other members
of the genus heterophyes, is provided with a peculiar armament which
is a distinguishing feature. Immediately in front of the oral opening are
two alternating rows of spines, and projecting from the oral opening
is a scoop-like chitinous lip, with four minute needle-like processes on
its dorsal margin. There are pairs of cephalic glands in the centre of
the body. The cercaria, on emerging from the snail, swims until it finds *Second inter-*
an appropriate fish and penetrates beneath the scales into the flesh, *mediary host*
utilizing the cephalic gland secretions to digest the host's tissues: during
this process the tail is cast off. The commonest edible fish which is the
source of human infection for this fluke is *Plecoglossus altivelis*. On
eating such an infected fish, mammals, man, and birds become infected.

(3)—Diagnosis

The diagnosis of metagonimus infection is made by the presence of the
appropriate eggs in the faeces. They can only be distinguished from
those of *H. heterophyes* by careful measurements.

(4)—Treatment
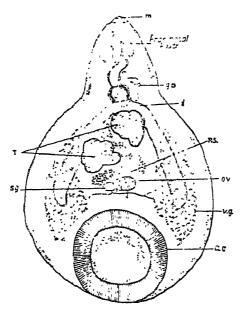
As in the case of heterophyes infection, the adult trematodes are
evacuated from the bowel, but they can also be removed by thymol,
betanaphthol, and carbon tetrachloride in therapeutic doses. Large
doses of magnesium sulphate expel considerable quantities.

7.—GASTRODISCOIDES HOMINIS

502.] *Gastrodiscoides hominis* (Lewis and McConnell, 1876) Leiper, 1913, *Geographical*
an amphistome fluke first found in 1876, was not accurately described *distribution*
until 1913 (Leiper). It has been found in numbers in the caecum
and ascending colon in India, Assam, Cochin China, and in Indian
immigrants in British Guiana. It is said to be a common parasite of the
pig in Assam, and it has also been found in the Napu deer (*Tragulus
napu*) from the Malay States.

Gastrodiscoides hominis is orange-red in colour. The body is formed *Morphology*

of an anterior conical portion and a posterior discoidal region. It varies in length from 5 to 10 mm. and from 4 to 6 mm. in cross section. There is a prominent genital cone situated half-way along the ventral aspect of the conical portion. The acetabulum is situated in the caudal portion of the body. There are no spines on the integument. The mouth opens into a globular oral sucker, and at its constricted posterior margin is a pair of lateral pouches. There is a pharyngeal bulb in front of the origin of the intestinal caeca, which extend to the middle region of the disc, where they end blindly. The genital organs are situated for the most part in the disc. The testes are large lobate organs situated near the anterior margin of the disc. The male duct opens on the summit of the genital cone just below the female pore. The rounded ovary lies in the centre of the disc. The vitellaria, or yolk glands, consist of small particles near the lateral margins of the disc. The uterus, arising from the shell gland, coils outwards and upwards. (See Fig. 74.)

FIG. 74.— *Gastrodiscoides hominis* (× 15). *m.*, mouth; *T.*, testes; *s.g.*, shell gland; *g.o.*, genital opening; *i.*, intestine; *R.S.*, receptaculum seminis; *ov.*, ovary; *v.g.*, vitelline glands; *ac.*, acetabulum. (After Khalil, *Proceedings of the Royal Society of Medicine*)

Eggs

The eggs are operculated and measure 150 to 152μ in length by 60 to 72μ in breadth. The life history of this fluke outside the human body is unknown.

Pathology

The fluke lies attached to the mucosa of the caecum and ascending colon, in which it causes local inflammation. The only attendant symptom is intermittent diarrhoea, but very few observations on this point seem to have been made.

Treatment

No one appears to have studied the question of treatment. It is probable, however, that carbon tetrachloride in doses of 60 minims would rid the body of this infection.

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FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

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Reference may be made to articles dealing with individual diseases, organs, and systems and also to the following titles:

DWARFISM AND   HEREDITY AND CONSTITUTION
INFANTILISM   SEX HORMONES

1.—DEFINITIONS

503.] A foetal disease is a morbid condition of the foetus starting at a *Foetal* time when the various bodily parts and organs have already been formed, *disease*

i.e. after the sixth week of intra-uterine life. It is caused by agencies similar to those which produce disease in postnatal life, namely, the various organisms and toxic substances which find their way to the foetus through the placental circulation, and may either progress or regress after birth (see p. 337).

Deformity   If the disease is of such a nature as to mutilate an already formed part of the foetus, such mutilation is called a deformity, e.g. the distortions produced by amniotic adhesions or the intra-uterine amputations brought about by tight cord-like amniotic bands.

Malformation   A malformation on the other hand is an abnormal formation of a part not yet fully developed and is due to an arrest—total or partial—or exaggeration of the normal development of some part of the body during the embryonic or organogenic period, namely, during the first six weeks after conception. Examples are: hare-lip and cleft palate, and spina bifida, which are due to failure of certain parts to grow together; anencephaly, due to failure of the brain to develop; and polydactyly *Monsters and* and macrodactyly, due to excessive growth of a part. When the dis-*monstrosities* figurement so produced is extreme it becomes a monstrosity, and the foetus is then called a monster. Thus, whereas hare-lip and syndactyly are malformations, anencephaly and dicephaly are monstrosities. The difference therefore between a malformation and a monstrosity is one of degree rather than of kind.

Congenital Though every foetal disease from which the foetus has not recovered *disease* before birth is congenital, not every congenital disease is necessarily foetal, in as much as it may have been only potentially present in the foetus without becoming manifest until some time after birth. This is the case with most of the hereditary diseases, such as diabetes mellitus, pseudo-hypertrophic muscular dystrophy, and acholuric family jaundice. Moreover, some diseases with which a child is born may have been acquired in the process of birth. These, like ophthalmia neonatorum and birth palsies, will not be alluded to in this article, and of the congenital abnormalities which are later postnatal manifestations of potential foetal diseases only those will be considered which appear during the neonatal period, namely, within the first month after birth, e.g. congenital obliteration of the bile-ducts.

2.–CLASSIFICATION OF FOETAL ABNORMALITIES

504.] Foetal abnormalities may be classified as follows:

Diseases   1. *Foetal diseases*

(i) Morbid conditions produced in the foetus by the placental transmission of organisms or toxins, e.g. syphilis, the exanthemata, tuberculosis, malaria, lead, or alcohol; or foetal nutritional diseases due to excessive or defective transmission of nutritive material or of hormones from mother to foetus, e.g. gigantism and nanism (dwarfism).

(ii) Idiopathic diseases of the various bodily systems.

(iii) Neoplasms. Many of these really come under the heading Malformations.

2. *Deformities due to amniotic adhesions*   *Deformities*

3. *Malformations*   *Malforma-*
                                                             tions
(i) Single, i.e. those affecting a single foetus. These may be due to:
(*a*) arrest of development of parts, e.g. achondroplasia, osteogenesis imperfecta, hare-lip, spina bifida; (*b*) excess of development of parts, e.g. local gigantism, polydactyly, polymastia; (*c*) errors of development, e.g. complete transposition of the viscera; (*d*) displacement of tissues and persistence of foetal structures, e.g. branchial cysts, dermoids, hermaphroditism.

(ii) Double, i.e. those affecting two foetuses joined together. These will be classified in greater detail later (see p. 377).

(iii) Triple, i.e. those in which there is evidence of union between three separate foetuses.

3.—FOETAL DISEASES

505.] Foetal diseases may be due to placental transmission of organisms and other substances, or to abnormal placental nutrition.

(1)—Placental Transmission of Organisms and Filterable Viruses

Normally the placenta prevents the transmission of deleterious agents from mother to foetus. Sometimes, however, these agents by damaging the placenta break down this physiological barrier and pass from the maternal into the foetal circulation.

(*a*) *Syphilis*

The *Treponema pallidum* is the organism which is most commonly conveyed to the foetus. Congenital syphilis, probably the most potent single cause of antenatal death, is dealt with elsewhere (see SYPHILIS).

(*b*) *The Exanthemata and other Infections*

Smallpox is, next to syphilis, the best known example of a disease *Smallpox* transmitted from mother to foetus. Exposure of a pregnant woman to smallpox results in one of the following events: (1) Both mother and foetus may escape infection. (2) The mother may contract the disease and the foetus may (*a*) be killed and expelled; (*b*) be born dead or alive with a smallpox rash; (*c*) be born alive with smallpox scars, showing that it had recovered from an attack of smallpox (Feldman, 1930); (*d*) be born without smallpox and either escape altogether or develop the disease soon after birth. In the case of multiple pregnancy, one or more foetuses may be born with evidence of present or past smallpox, the others escaping infection and remaining either susceptible or insusceptible to vaccination—in the latter event because of the placental

Prophylaxis transmission of antibodies. Prophylaxis consists in vaccination of the expectant mother during an epidemic or after exposure to smallpox.

Measles Measles very rarely occurs in the foetus, because the mother, having generally had the disease, not only is insusceptible to infection but transmits immune bodies to her baby. A mother suffering from measles, however, may transmit the disease to the foetus. Foetuses have been born with oculo-nasal catarrh, Koplik's spots, and a raised temperature, followed by the characteristic rash very soon after birth, or with the rash present at birth. It is impossible to tell whether or not a foetus has successfully recovered from an attack in utero, measles differing in this respect from smallpox, but some children who remain permanently immune to the disease may be examples of such an event. That antibodies of measles pass from mother to foetus is probable from the fact that most infants—even those that are bottle-fed and therefore do not receive such immune bodies from their mother's milk—remain immune to

Prophylaxis measles during the first few months. A susceptible mother should not be exposed to infection, and an infant born to a mother with measles will, unless protected, probably succumb to an attack of the disease. It should therefore receive an injection of convalescent measles serum and be allowed to be nursed by its mother.

Scarlet fever Scarlet fever in the foetus is also very rare, but several cases have been recorded. Liddell and Tangye described two cases in new-born babies: one had tonsillitis followed by an eruption and the other showed the characteristic desquamation. In each case the mother had, towards the end of pregnancy, been nursing children affected with the disease. As in the case of measles, the mother may also transfer immunity to her unborn infant, and most authorities agree that the infant of a mother suffering from scarlet fever should be allowed to be nursed by its mother.

Diphtheria Foetal diphtheria is exceedingly rare, the *Corynebacterium diphtheriae* being apparently unable to pass the placental barrier. On the other hand immune bodies are transmitted through the placenta, as would appear from the negative response of most new-born babies to the Schick test. It would seem, however, that the Schick test is not quite reliable in new-born infants because of the difficulty of making in them a truly intradermal injection. This is seen from the fact that such infants sometimes give a negative result even when antitoxin is absent from their blood. To be on the safe side therefore an infant born of a mother with diphtheria should receive an injection of antidiphtheritic serum and be allowed to be nursed by its mother. A case in which the bacillus was found in the peritoneal fluid of a still-born foetus whose mother had recovered from diphtheria was recorded by Traugott (1926).

Chicken-pox Foetal chicken-pox has been recorded in the case of a baby born to a woman who had been exposed to the disease fourteen days previously without contracting it; the baby had the polymorphic rash characteristic of the fourth day of the disease, showing that it had contracted the disease before birth.

Typhoid Typhoid fever in the pregnant woman kills the foetus in about 65 per

cent of cases, and from the tissues of such dead foetuses *Bacterium typhosum (Bacillus typhosus)* has been isolated. Of those that survive some develop the disease very shortly after birth, as shown by the presence of the bacillus in their blood and in the blood of the umbilical cord, as well as by a positive Widal reaction and the presence of bacilli in the stools. A positive Widal reaction alone in a new-born baby is not evidence of recovery from an intra-uterine attack of the disease, since it may simply indicate the transmission of agglutinins from mother to foetus.

The organisms of erysipelas, anthrax, cholera, and undulant fever *Other diseases* have also been detected in the foetus, and apparently authentic cases of acute foetal rheumatism have been described (Richdorf and Griffith; Kissane and Koons).

(c) Pneumonia

The pneumococcus is transmitted from a mother suffering from pneumonia and kills the foetus in 66 per cent of cases. Of the foetuses that survive some develop either pneumonia or pneumococcal septicaemia, from which they die.

Expectant mothers should not visit or be visited by any person having *Prophylaxis* a cold, or by anyone in attendance on a pneumonia patient, or any person convalescent from pneumonia, since they may be carriers of a virulent strain of the pneumococcus. Pregnant women should avoid exposure to damp and cold, and any respiratory infection, however slight, should be treated by rest in bed, warm drinks, and proper nursing. When contact with a member of the household suffering from pneumonia is unavoidable, the woman should receive four weekly doses of pneumococcal vaccine, the first dose to contain 1,000,000,000 each of types i, ii, and iii pneumococci, the second and third injections twice that amount, and the fourth dose four times that amount (Cecil and his co-workers).

(d) Influenza

Many infants born to infected mothers during the 1918–19 influenza epidemic showed signs of the disease and succumbed to bronchopneumonia, although it has not been definitely established whether the disease was contracted in utero or immediately after birth. The probability of transplacental infection is illustrated by a case recorded by Abt.

(e) Encephalitis Epidemica

The virus of encephalitis epidemica has been shown experimentally in animals, and clinically in human beings, to pass through the placenta.

(f) Malaria

Foetal malaria, though denied by many, undoubtedly occurs; Wickramasuriya recently recorded six cases in which he found the plasmodium

in the foetus. Unless the foetal blood contains more than 50 parasites per c.mm., i.e. more than about 11,000,000 parasites in the whole of its blood, it may not show any clinical evidence of malaria, but such an infant may soon after develop malaria, if the rate of multiplication of the parasites becomes rapid. On the other hand, if the resistance of the foetus is great, the parasite may die; this explains the failure of some observers to find the plasmodium in the foetal blood. A malarial mother may give birth to a dead foetus, as a result of the massive infection of the placenta with the plasmodium, the hyperpyrexia, or the direct infection of the foetus, or to a live feeble infant which dies soon after, or to one with signs of the disease, namely, pyrexial attacks followed by sweating, splenic enlargement, and the presence of the plasmodium in its blood. A case of foetal malaria with the parasite in the blood has also been recorded as the result of malarial treatment of a tabetic expectant mother.

Prophylaxis   Malarial expectant mothers should receive full doses of quinine, 5 to 10 grains three times a day, which in such cases does not act as an oxytocic but, on the contrary, prevents premature labour in the same way as mercury, which acts as an abortifacient in healthy women, prevents and cures foetal syphilis in syphilitic women. According to Manson-Bahr, atebrin (an allyl amino-acridine derivative) is better tolerated by pregnant women. It is given in $4\frac{1}{2}$ grain doses for ten days. It is remarkable that, whereas in non-malarial countries the neonatal mortality has been stationary, in tropical countries in which malarial expectant mothers receive adequate quinine therapy it has greatly fallen because of the decline in the birth-rate of premature and debilitated infants. (Personal communication from Dr. S. Eveson, Health Officer of Singapore.)

(g) Tuberculosis

Foetal tuberculosis, although extremely rare, undoubtedly occurs, as shown by the discovery of tubercle bacilli or disseminated miliary tuberculosis in still-born foetuses, when the question of early postnatal infection does not, of course, arise (Whitman and Greene).

Modes of transmission   The disease may be transmitted to the unborn child in a number of ways:

Infection of ovum or sperm   a. Germinal infection. (1) The ovum may contain the bacillus before it is fertilized. (2) The bacillus may enter the ovum with the fertilizing spermatozoon, to which it has become attached in its course from the testicle through the male and the female genital tracts until it reaches the ovum in the Fallopian tube. Semen from a tuberculous patient has produced tuberculosis when injected into animals. Germinal infection may also occur as the result of lubricating the penis before coitus with sputum laden with tubercle bacilli (Cornet). On the other hand it is contended that germinal infection cannot produce foetal tuberculosis, because an ovum so infected would be killed before it began to segment.

b. Trans-placental infection as the result of maternal bacillaemia. In

about 7 per cent of cases the injection of blood of tuberculous patients *Infection* into guinea-pigs produced tuberculosis, showing that the blood of *from blood* tuberculous patients may contain the organisms. These organisms may therefore pass to the foetus either by first infecting the placenta or, as has been maintained by some, through a healthy placenta.

c. Direct infection of the placenta from a tuberculous uterus.   *From uterus*

d. Placental transmission of the ultravirus phase of the *Myco-* *Ultravirus* *bacterium tuberculosis*. Fontes (1910) first showed that the Chamberland *phase* filtrate from a tuberculous abscess, though devoid of bacilli, nevertheless produced tuberculosis when injected into animals, and that ripe bacilli could be subsequently isolated from them. That such a virus can pass from mother to foetus has been shown by the fact that tuberculosis with lesions from which acid-fast bacilli have been isolated has been produced in animals inoculated with the umbilical blood of a foetus of a tuberculous mother, although neither tuberculous lesions nor acid-fast bacilli could be found in the placenta. Many authorities deny the existence of such an ultravirus, whereas others believe that such a virus does exist, but that instead of producing foetal tuberculosis it confers immunity upon the foetus during its early postnatal life. At any rate, the facts that the vast majority of infants immediately separated from their tuberculous mothers do not develop tuberculosis, and that of the many such infants tested with tuberculin none reacted positively, militate against the existence of such a virus. Most cases of so-called congenital tuberculosis are really cases of early neonatal infection (Kayne).

(2)—Placental Transmission of Toxic Substances

(a) Alcohol

Alcohol has been found in the blood of foetuses of inebriate mothers, and experiments on animals have shown the teratogenic effects of alcohol upon the foetus not only during its developmental stage but also through its deleterious effects upon the spermatozoa. Its effect in human pathology has been disputed, but the following figures are interesting: a healthy woman had six normal children by her first husband; after her second marriage, with a drunkard, she had three premature babies, of which one died at birth and both of the other two had meningocele and polycystic kidneys. The subject is fully dealt with elsewhere (Feldman, 1927, a).

(b) Morphine

Morphine has been found in the blood of a foetus of an addict mother, although recent experiments on addicted dogs failed to show traces of the drug in their puppies which were quite healthy. It is maintained *Signs of* that the infants of morphine addicts show clinical evidence of addiction, *addiction in* *infants* namely, restlessness, yawning, jerkiness, and even sudden collapse, and it has been recommended that such infants should not be suddenly deprived of the drug but should be given small doses until placed on their mother's breast, when they will receive the drug through the milk.

On the other hand, many authorities deny the presence of morphine either in foetal blood or maternal milk, or of any signs of addiction in the new-born. The statistics collected by the American Committee on Drug Addictions (1921) favour the first view, and it would seem that the proper procedure is to allow such an infant to be put to the mother's breast as soon as possible, and to start weaning it gradually as early as feasible (Terry and Pellens).

(c) Cocaine

Effect on foetus

Cocaine has a deleterious effect upon the foetus, as shown by the following observation by Marfan: in a family of four children the first, born before the father became a cocaine addict, was perfectly normal at the age of twelve; the second, conceived two months after the habit began, was at the age of eight years puny and mentally backward, and the two children conceived after the habit was firmly established were complete idiots, the younger one being microcephalic.

(d) Nicotine

Workers in tobacco factories

Nicotine is alleged to have been found in foetal blood when the mothers were excessive smokers, although statistics collected in large tobacco factories fail to show an abnormally large number of abortions or of defective foetuses among children of the women workers. In the breast-fed dyspeptic baby of a woman who was an excessive smoker I did not find nicotine in its mother's milk to account for the dyspepsia.

(e) Lead

Paternal plumbism

The abortifacient effects of lead are well known, and the metal has been found in the still-born children of female lead-workers. Paternal plumbism has also a deleterious effect upon the foetus, and J. Thomson recorded cases of typical saturnine convulsions in two new-born infants whose father, but not the mother, suffered from plumbism.

(f) Pregnancy Toxin

Lesions similar to those found in eclamptic mothers have been demonstrated in the livers of their foetuses.

(3)—Placental Transmission of Malignant Disease (Sarcoma)

An interesting case of the transmission of sarcoma from the mother to the foetus has been recorded (Weber, Schwarz, and Hellenschmied). The mother had had sarcoma during pregnancy and the placenta showed sarcomatous deposits. The infant developed the condition in the first weeks of life and died at the age of ten months.

(4)—Disorders of Placental Nutrition

Foetal gigantism

Abnormal size of placenta

For optimum foetal nutrition there is normally a fairly definite relation between the size of the foetus and the functional surface area of the placenta. If the placental size is increased, or if the maternal blood contains an excess of nutritive material, the foetus may grow abnormally

large (foetal gigantism). If the opposite condition prevails, the foetus *Maternal* may be abnormally small. In maternal hyperglycaemia therefore the *hyper-glycaemia* foetus may be abnormally heavy, because it receives a large amount of carbohydrates, transmitted osmotically, which are the source of foetal fat. The largest foetuses reported, however, were born to non-diabetic, normal-sized mothers. E. L. Moss (1922) recorded a female foetus weighing 24 pounds 2 ounces and measuring 35 inches in length, the average for a child eighteen months old (see Fig. 75). The mother was twenty-two years old, and her birth passages were sufficiently large to allow the normal birth, although the foetus was still-born. The condition, unless very pronounced, cannot easily be diagnosed, but if it is suspected, especially in cases of great post-maturity, the proper treatment is Caesarean section. In hyperglycaemia the condition should be prevented by antidiabetic treatment during pregnancy. In other cases it cannot be prevented, since the placental transmission of minerals, upon which the size of the foetus chiefly depends, is probably a vital rather than an osmotic process as shown by the difference in the mineral concentration

FIG. 75.—Foetus, weight 24 pounds 2 ounces: length, vertex to heel, 35 inches. (*Proceedings of the Royal Society of Medicine*, 1929)

between the maternal and the foetal bloods; restriction of minerals in the maternal diet can therefore make very little difference to the size of the foetus.

Defective transmission of vitamins may result in deficiency diseases *Foetal* in the foetus. Maeda met with several cases of mild beri-beri in new-born *deficiency* *disease* infants; Jackson and Park described an undoubted case of foetal scurvy; and Maxwell and Turnbull described two cases of true rickets in the foetuses of mothers suffering from osteomalacia.

Abnormally small foetuses are of different kinds. Those due to pre- *Small* maturity do not as a rule survive if born before the twenty-eighth week. *foetuses* Small foetuses due to immaturity (i.e. under-sized for foetal age) may be of very small dimensions. I have seen a premature and immature baby which was born at twenty-six weeks, weighed 1¾ pounds and measured 13 inches in length; the child is now (1937) a normal-sized

Dwarfism

girl sixteen years old and of average mental development. On the other hand, there may be cases of true dwarfism in which postnatal growth is also retarded. Such a condition is called nanism (νᾶνος, a dwarf), microsomia (μικρός, small; σῶμα, body), or ateleiosis (ἀτελείωτος, imperfect). Nicholas Ferry Bébé, born in the Vosges in 1741, was such a dwarf. His weight and length at birth are said to have been 14 ounces and 9 inches respectively, and at the age of fifteen he was only 29 inches tall. Such true dwarfism, in which the bodily proportions are perfect,

False dwarfism

must be distinguished from false dwarfism due to achondroplasia. True female dwarfs may present a considerable problem to the obstetrician on account of their generally contracted pelvis (pelvis nana).

Inheritance of dwarfism

Although true dwarfism tends to recur in several children of the same parents, the children of two dwarf parents are not dwarfs. Robert Skinner (25 inches) and Judith (26 inches) had fourteen infants, well formed and of normal length (Gould and Pyle). According to Cockayne, the condition is probably due to two independent genes. (See also DWARFISM AND INFANTILISM, Vol. IV, p. 277.)

4.–AETIOLOGY OF MALFORMATIONS AND MONSTROSITIES

Mendelian inheritance

506.] Many malformations and monstrosities, such as polydactyly, cleft palate, achondroplasia, complete visceral transposition, and anencephaly behave like Mendelian hereditary characters.

Poisons and toxins

Most of the others, however, judging from analogy with what is known to occur experimentally in the case of developing avian and aquatic eggs on injecting alcohol or other poisons into them, most probably result from the action of poisons or toxins on the gametes before conception, or on the developing fertilized ovum through the contaminated blood from which it receives its nourishment.

Defective oxygenation

Thus abnormal nidation, as in ectopic pregnancy, may result in an insufficient supply of oxygenated blood to the foetus and so cause abnormal development. Hence, although several cases have been recorded of extra-uterine pregnancy going to full term with the delivery of normal foetuses, in a very large proportion of such cases (96 per cent, Mall) the foetuses or embryos are abnormal. Similar defective oxygenation may occur in advanced maternal cardio-respiratory diseases.

Toxins

The toxins of syphilis and tuberculosis, alcohol, or lead circulating in the maternal blood are other theoretical teratogenic agents, although statistics have not shown an excessive number of malformations in syphilitic foetuses.

Pyrexia and X-rays

High intra-uterine temperatures, as in prolonged pyrexial diseases, and frequent exposures of the mother to X-rays during the early period of gestation may also exert deleterious effects upon the embryo or foetus. Several cases of anencephalic foetuses born to mothers exposed to X-rays early in pregnancy have been recorded (see p. 385).

Mechanical factors, such as foetal compression due to oligohydramnios *Mechanical* or fibroids are doubtful causes; Denis Browne, however, believes that *factors* such compression is responsible for congenital talipes equinovarus, acrocephalosyndactylism (oxycephaly), and even some intra-uterine fractures. This hypothesis has not in my view been fully substantiated.

Foetal inflammatory conditions are also probable causes: for example, *Inflammation* foetal endocarditis may play a part in congenital heart disease, foetal peritonitis may be responsible for various intestinal or biliary strictures, and foetal myositis for congenital torticollis.

Amniotic adhesions (see Fig. 76) *Amniotic* produce very serious deformities, *adhesions* mutilations, and some intra-uterine amputations; some, however, of the so-called amputations, such as hemimelia (absence of whole or parts of limbs), are undoubtedly of germinal origin. Tight loops of the umbilical cord cannot cause such amputations, since loops so tight must necessarily stop the circulation in the cord and kill the foetus before producing the amputation.

From analysis of 132 malformations and deformities among 10,000 births Unterrichter found that in nine cases certainly, and in another seven cases most probably, heredity played a part. Thus, *Heredity* cleft palate, sacral meningoceles, phimosis, syndactyly, microphthalmos, pyloric stenosis, and anencephaly appeared in different children born to the same mother

Fig. 76.—Union of amnion with head; abnormally short cord. (This and Figs. 77, 78, 88, and 90 from *Diseases of the Foetus* by Birnbaum and Blacker)

or father or in collaterals of a family. Indeed it is known that some malformations, such as polydactyly and syndactyly, behave like Mendelian dominants or recessives, and I have shown that complete visceral transposition is a Mendelian recessive character; in one such case the parents were first cousins and, although themselves normal, at least three out of their twelve children had their viscera completely transposed (Feldman, 1935). Unterrichter doubted if maternal gynaecological conditions played any teratogenic part.

It may at first seem that conditions such as anencephaly or intestinal atresia, which are incompatible with postnatal life and hence with survival to the reproductive period, cannot possibly be hereditary; but

such inheritability may, according to Cockayne, be explained on the
supposition that a 'mutation' had occurred in the gametic chromosomes
of the ascendants of each of the parents of such abnormal foetuses,
which subsequently behaves like a Mendelian recessive tending to
bring about the abnormality in the offspring (see p. 370). The cause
of such a mutation is unknown, but it might be a circulating toxin, as
in syphilis, alcoholism, or lead poisoning. See also HEREDITY AND
CONSTITUTION.

5.—ABNORMAL CONDITIONS OCCURRING IN DEAD FOETUS

507.] The dead foetus may become macerated or, more rarely, mum-
mified (foetus papyraceus); but the most interesting, although the rarest,

Petrifaction

FIG. 77.—Stone child

condition is that of petrifaction
resulting in a lithopaedion or
'stone child' (see Fig. 77). This
change, which generally occurs in
a dead extra-uterine foetus, may
also occur in one which died in
utero. The dead foetus, instead of
being expelled, remains in utero
indefinitely, the liquor amnii be-
comes absorbed, and lime salts are
deposited around the foetus, con-
verting it into a stony hard mass,
which the woman feels shifting
about as she changes her position.
The diagnosis is made from the
history of a pregnancy many years
previously which did not ter-
minate in abortion or labour, the
presence of a stony hard movable abdominal or pelvic tumour, and
the X-ray appearances which may show foetal bones. In many cases the
condition does not cause any symptoms, is not suspected during life,
and is accidentally discovered at necropsy in women who have died of
old age; Winckel recorded the case of a woman of eighty-four years
who carried a seven months' foetus in her right Fallopian tube for
fifty-six years, and a case in a centenarian was reported, with a radio-
graph, in 1936 by Lye. The foetus should be left alone unless it causes
symptoms, in which event it should be surgically removed.

Foetus
acardiacus   Another theoretically interesting, though very rare condition, is foetus
acardiacus, which is a more or less shapeless mass, the remains of one
of a pair of monochorionic (uniovular) twins, of which the other is
alive and healthy. It occurs as the result of free anastomosis between
the blood-streams of the two co-twins, when· the circulation of the

stronger foetus reverses the direction of the blood-flow in the weaker one, causing complete atrophy of most of its organs. What more commonly happens, however, is that the weaker foetus, though fully developed, dies as the result of stasis of its circulation produced by such reversal of flow. It is for this reason that death of one of the foetuses is much commoner in uniovular twins, between whom there is generally a free circulatory interchange, than in binovular twins, between whom such intercommunication seldom if ever occurs.

6.–ABNORMAL CONDITIONS OCCURRING IN LIVING FOETUS

(1)—Skin

508.] Lack of pigmentation. In partial lack of pigmentation, or vitiligo, *Vitiligo* there are scattered white unpigmented patches of skin and hair in different parts of the body. In complete lack of pigmentation or *Albinism* albinism, the whole skin is devoid of pigment, the hair is yellowish-white, and the irides are transparent, causing photophobia and nystagmus (see ALBINISM, Vol. I, p. 271).

Increased pigmentation, e.g. Mongolian spots and pigmented naevi. *Mongolian* Mongolian spots are bluish patches most commonly found on the *spots* lumbo-sacral region. They usually are present at birth or appear soon after birth and do not affect the physical or mental health of the child. Although most common in Mongolian races, in which they occur to the extent of some 80 per cent, they are also met with in white races, to the extent of some 5 per cent, and therefore should not throw any suspicion on the legitimacy of a white baby so affected. They hardly ever occur in cases of mongolism. No treatment is necessary as the spots generally disappear spontaneously in later childhood.

As far as anatomical, physiological, embryological, and statistical *Angiomas* considerations show, naevi are not related to 'maternal impressions' received during pregnancy. The condition is described under the title ANGIOMA, Vol. I, p. 577.

Vascular naevi (haemangiomas and telangiectases) may not only grow *Haem-* and cause great disfigurement, but are liable to injury resulting in *angiomas* dangerous bleeding. They therefore require immediate energetic treatment by excision, cauterization, or radium.

Closely allied to haemangiomas are lymphangiomas, which are con- *Lymph-* genital dilatations of the lymphatics. They generally involve the upper *angiomas* limb and may be large enough to cause dystocia (see Fig. 78). A child born alive may continue to live, but treatment is impracticable. The condition is often called congenital elephantiasis, but a streptococcus rather than filaria is the organism generally found, and the condition may occur in non-tropical countries. Congenital cystic elephantiasis, *Congenital* i.e. cystic swellings of the skin all over the body with lymphatic enlarge- *cystic* *elephantiasis* ment, is generally fatal immediately after birth. Cystic hygroma of the *Cystic* neck, which may be large enough to cause difficult labour, is also a *hygroma*

lymphangioma and may be confused with branchial cysts (see NECK, TUMOURS AND OTHER MORBID CONDITIONS), or thyroglossal cysts (see p. 359). The treatment, if the swelling continues to grow, consists of complete removal preceded by radium-therapy to render recurrence less likely. Removal may be difficult, but, if it is not carried out, the hygroma may recur. Harrower recorded a successful cure of cystic hygroma in an infant one month old by the injection of a 5 per cent solution of sodium morrhuate.

For lymphangioma circumscripta see SKIN TUMOURS.

Hydrops foetalis

Hydrops foetalis or general foetal dropsy is characterized by general anasarca and fluid in most of the serous cavities, such as the peritoneum (ascites), pleura (hydrothorax), pericardium (hydropericardium), tunica vaginalis (hydrocele), and sometimes even in the subarachnoid spaces (producing hydrocephalus). It is usually accompanied by great oedema of the placenta and results in antenatal, intranatal, or early postnatal death of the foetus or infant. The condition, which generally occurs among the later foetuses of multiparae, tends to be familial, in as much as not only may successive foetuses born to the same woman be similarly affected, but also foetuses of unrelated women whose husbands are brothers. The foetal enlargement may be sufficient to cause dystocia and even

FIG. 78.—Diffuse lymphangiomas causing obstruction to delivery (after Ahfeld)

maternal death from exhaustion due to prolonged labour, but is said never to have caused rupture of the uterus. The labour, however, may be easy on account of prematurity as well as reduction of the foetal size resulting from oozing from the broken skin brought about by intranatal compression. The placenta is large and oedematous and, from the contained fluid, may weigh as much as the foetus. Owing to the size of the placenta and to the uterine inertia resulting from the prolonged second stage of labour the third stage may be difficult. If the foetus escapes antenatal or intranatal death, it dies soon after birth from impairment of the circulation produced by the hydropericardium, or from asphyxia due to compression of the lungs by the hydrothorax and restricted movements of the diaphragm caused by the ascites. Because of their sodden state the skin and other tissues are friable. The effusion is usually serous, though it may be gelatinous; and it contains albumin but not sugar.

Aetiology

The familial incidence of hydrops foetalis points to a germinal cause. It may, however, be due to abnormal conditions of the mother, such

as nephritis, hydramnios, and alcoholism, or to morbid states in the foetus, which mechanically produce the dropsy. According to Ballantyne it is not due to maternal syphilis. The foetal conditions are: cardiac abnormalities interfering with the venous circulation; absence of the ductus venosus; diaphragmatic hernia compressing the inferior vena cava; hepatic cirrhosis compressing the portal vein; renal hypoplasia; chronic foetal peritonitis; foetal diseases of the blood and haemopoietic organs (see foetal erythroblastosis below, and erythroblastaemia, Vol. I, p. 462).

Antenatal diagnosis is practically impossible, although the condition *Diagnosis* may be suspected in a dropsical albuminuric mother with hydramnios, who has previously borne a dropsical foetus. Intranatally, the diagnosis is made from the condition of the skin of the presenting part, which is friable and oozes fluid.

Any obstetric difficulty due to excessive size is overcome by aspirating *Intranatal* the fluid from the skin, peritoneum, or thorax. If this is not enough, *treatment* embryotomy should be done.

Foetal erythroblastosis, first described by Schridde in 1910, is a form *Foetal* of foetal dropsy associated with a morbid state of the blood and *erythro-* *blastosis* haemopoietic organs. In addition to the dropsy, the blood, as well as the spleen and liver, which are enlarged, contain an excess of erythroblasts. The disease had been erroneously described as congenital leukaemia until Schridde recognized its true nature. The name erythroblastosis was given to it by Rautmann.

Foetal ichthyosis may be of different degrees of severity. In the most *Ichthyosis* pronounced cases (see Fig. 79) the foetus is completely covered with horny plates separated by furrows crossing one another in different directions (harlequin foetus). If born alive, the baby dies within a few days from hypothermia due to defective metabolism, inanition, and defective development of the heat centre, as well as from starvation owing to oral rigidity and the consequent difficulty of feeding. Mild conditions are compatible with life and should be treated by means of warmth and inunctions with oil, to which should be added some salicylic acid, 10 to 15 grains to the ounce, to help removal of the scales. The condition is familial.

Erythrodermia desquamativa of Leiner, an erythema followed by *Erythro-* scaling, may be erroneously diagnosed as ichthyosis. Differentiation is *dermia* *desquamativa* desirable, because Leiner's disease is not necessarily fatal and may completely disappear. The most important diagnostic feature is that Leiner's disease always appears after birth and is never present at birth.

Sclerema neonatorum, a diffuse induration of the skin over large areas *Sclerema* of the body, is distinguished from foetal dropsy by absence of pitting *neonatorum* on pressure. Death occurs as a rule very soon from inanition and hypothermia.

Sclerodermia neonatorum consists of isolated, irregularly distributed *Sclerodermia* solidified plaques which tend to disappear as the baby grows older. *neonatorum*

In view of the great difference in prognosis it is important to distinguish it from sclerema. Treatment is useless in sclerema and unnecessary in sclerodermia.

Absence of skin

Absence of skin may occur in certain parts (see Fig. 80). When the defects are small they are usually of very little clinical importance, since postnatal healing occurs fairly soon without in any way affecting the health of the infant. Indeed in some cases the presence of superficial scarring at birth shows that healing had taken place in utero. Other cases show both open and scarred lesions at birth. A case of scarred congenital skin defect in one of a pair of binovular twins, the other being normal, was recorded by Bazal. If the defect at birth is extensive, healing takes a long time and may undermine the baby's health. Treatment consists in keeping the denuded areas clean and free from irritation. The condition may be either of germinal origin or due to amniotic adhesions.

Skeleton baby: india-rubber baby

More rarely the subcutaneous fat alone is absent, producing immobility of the skin (skeleton baby) as the result of the adhesion of the skin to the deeper-lying fascia; and equally rarely, the elastic and fibrous tissues of the true skin may be so fine and elastic as to produce excessive mobility (india-rubber baby).

FIG. 79.—Foetal ichthyosis; 'harlequin foetus' (From *Diseases of the Newborn* by von Reuss)

Congenital tumours of the skin are discussed under the title SKIN TUMOURS.

Congenital alopecia or hypotrichosis may be complete or partial. In the complete form the scalp is bald and eyebrows and eye-lashes are absent. In the partial variety only some parts are devoid of hair. The condition, which is probably a Mendelian character, may either persist throughout life or may spontaneously disappear. (See also ALOPECIA, Vol. I. p. 341.)

Hypertrichosis or excessive hairiness (gorilla baby) may be present at birth and is probably a germinal condition.

Poliothrix circumscripta is a congenital absence of pigment in certain tufts of hair.

Anonychia or absence of nails also occurs and is a Mendelian character. Frequently anomalies of the nails and hair occur together and may be accompanied by deficiency of function of the sweat, sebaceous, and lacrimal glands, as well as other malformations. (See also NAILS DISEASES.)

FIG. 80.—Congenital absence of skin. (This and Figs. 86 and 87 from *La Pratique de l'art des accouchements*, edited by A. Brindeau)
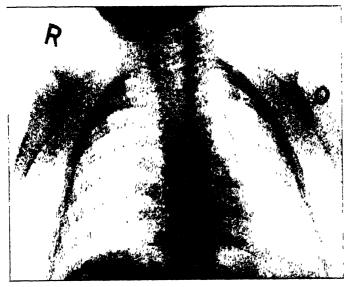
FIG. 81.—Complete absence of clavicles, radiographic appearances. Dr. R.C. Jewesbury's case. (This and Fig. 82 from *Proceedings of the Royal Society of Medicine*, 1937)

(2)—Skeleton

(a) Absence of Bones

Of the long bones the radius is the one most commonly absent, but the tibia, fibula, humerus, or femur may be missing (see BONE DISEASES, *Cleido-cranial* Vol. II, p. 558). The most interesting condition is cleido-cranial dys-*dysostosis* ostosis, in which there is bilateral, partial or complete absence of the

clavicles with defective ossification of the frontal bones (see Fig. 81). The infant's arms can be brought together in front of the chest (see Fig. 82). The fontanelle remains open until adolescence, and there is delayed eruption of the permanent teeth. The condition is compatible with life and intelligence, is incurable, and seems to be a Mendelian character. A pedigree showing incidence of the abnormality in several members of each of three generations was given by Langmead (1916). (See also Vol. II, p. 556.) A case recognized in an infant one day old was described by Higgins. The condition should be suspected in a new-born infant having very large fontanelles but not hydrocephalus.

Amelia
Ectromelia

Amelia (α, privative, and μέλος, limb) means absence of all limbs. Ectromelia (ἔκτρωσις, a miscarriage) is absence of one or more limbs. When the upper limbs are absent, the person may train himself to do with his feet all actions usually done by the upper limbs, e.g. feeding, sewing, shooting, and playing musical instruments. Such a person was exhibited a few years ago in Mills's Circus in London. Hemimelia or absence of the distal portions of one or more limbs is

Hemimelia

distinguished from true intra-uterine amputations

FIG. 82

Same case as in Fig. 81 by amniotic bands by the fact that such bands are not seen, the missing parts are not found in the amniotic cavity, and neighbouring bony deformities are found by means of X-rays.

Phocomelia Phocomelia (φώκη, seal) means absence of the proximal parts of a limb with attachment of the distal portion, such as hand or foot, to the trunk, giving the foetus a seal-like appearance (see Fig. 83). Oligo- or ectrodactyly is absence of one or more fingers. All these malformations are probably Mendelian characters.

Absence of vertebrae is occasionally met with in the lumbo-sacral *Klippel-Feil* region. A very interesting malformation is the Klippel-Feil syndrome, *syndrome* in which some or all the cervical vertebrae are missing. The baby therefore has either a very short neck or no neck at all, and the movements of its head are very much restricted.

Absence of the sacrum and coccyx is usually not recognized until the *Absence of* infant is grown up, when the outstanding features are: (i) atrophy of all *sacrum and coccyx* the muscles supplied by the sacral plexus, (ii) perianal anaesthesia, (iii) incontinence of urine and sometimes of faeces, (iv) absence of ankle jerks, and (v) discovery of the defect by rectal examination and by means of X-rays.

For further discussion see section on congenital bone dystrophies in BONE DISEASES, Vol. II, p. 554.

(b) *Defective Development of Bones*

General

Achondroplasia is dealt with elsewhere (see ACHONDROPLASIA, Vol. I, p. 135, and DWARFISM AND INFANTILISM, Vol. IV, p. 284).

Achondroplasia

Fragilitas ossium, including osteogenesis imperfecta and osteosclerosis fragilis generalisata (marble bones), is dealt with under BONE DISEASES, Vol. II, p. 554.

Fragilitas ossium

FIG. 83.—Phocomelus showing also umbilical hernia. (From *Antenatal Pathology and Hygiene, the Embryo*, by J. W. Ballantyne)

Partial

Failure of ossification of symmetrical portions of the two parietal bones produces congenital *Congenital* bilateral parietal foramina, which simulate patent fontanelles (see *bilateral parietal* Fig. 84). The condition persists throughout life, can easily be palpated *foramina* on the skull, and shows up with X-rays. It behaves like a Mendelian dominant (parent and child having the same abnormality) and is not at all uncommon, although often undetected because not looked for.

Anencephaly (absence of the cranial vault) is considered on *Anencephaly* page 369.

Spina bifida (spondyloschisis, or rachischisis) is dealt with under the *Spina bifida* title SPINAL CORD DISEASES.

(c) *Cleft Palate*

Hare-lip and cleft palate are considered under the title PALATE, *Cleft palate* CLEFT.

(d) Hemihypertrophy

Hemihypertrophy consists of a disproportion between the two sides of the body, the X-rays showing enlargement of all the bones on one side. The majority of the forty-four cases so far recorded have been in males. The condition is compatible with life, and its aetiology is unknown. It is discussed under the title HEMIATROPHY AND HEMI-HYPERTROPHY.

(e) Other Malformations of Limbs

Syndactyly   Syndactyly (fusion of fingers) and polydactyly (supernumerary fingers) are Mendelian dominants. The former condition is treated by a plastic
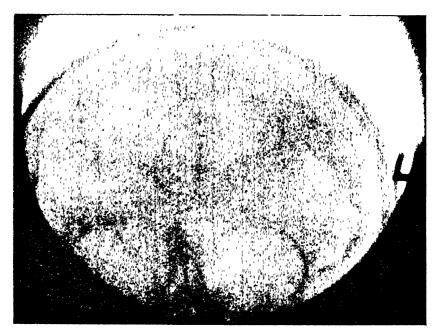
FIG. 84.—Congenital bilateral parietal formina. Dr. R. C. Jewesbury's case.
(Proceedings of the Royal Society of Medicine, 1936)

operation and the latter by amputation. The frequent association of syndactyly with oxycephaly (turret-shaped head) has led to the term acrocephalosyndactyly; this condition, which has occurred in mother and daughter, is almost certainly a linkage of dominant characters (see also Vol. II, p. 560, HAND, DISEASES, and OXYCEPHALY).

Radio-ulnar synostosis   Radio-ulnar synostosis (congenital pronation) is a fusion of the ends of the two bones of the forearm. This familial bilateral condition may not be recognized until the child gets older, when it is noticed that it cannot supinate the hands (see Vol. II, p. 559).

Symmelia   Symmelia (sympodia, sympus) or siren formation is a monstrosity in which the lower limbs are fused into a single structure, giving the foetus a mermaid-like appearance. It is accompanied by imperfect development of the pelvis and by atresia of the anus and urethra and is therefore incompatible with postnatal life.

Congenital hypertrophy of one or more fingers, macrodactyly, may *Macrodactyly*
occur. Arachnodactyly ('spider fingers'), in which the fingers and toes *Arachno-*
are extremely long and slender, is a Mendelian dominant and is *dactyly*
generally linked with another dominant character, namely, dislocation
of the lens (see Fig. 85). See Vol. II,
p. 557.

Clinically, the most interesting   *Club-foot*
malformations in the feet are the   *and*
varieties of club-foot; they are dis-   *flat-foot*
cussed under the title TALIPES. Flat-
foot, which is sometimes congenital,
is discussed under the title FOOT,
DISEASES AND DEFORMITIES.

For club-hand see HAND, DISEASES   *Club-hand*
AND DEFORMITIES.

(f) Anomalies of Ribs

Supernumerary ribs may be pre-   *Super-*
sent in the neck or in the lumbar   FIG. 85.—Arachnodactyly in a boy   *numerary*
region. On the other hand one or   aged 3¼ years. (St. Bartholomew's   *ribs*
more ribs may be absent or fused   Hospital Reports, 1920)   *Absent*
together, giving rise to scoliosis as   *ribs*
the child grows up. These conditions do not produce signs or symptoms
at birth and usually are only discovered accidentally if an X-ray ex-
amination of the chest happens to be made in early life. In adult life
cervical ribs may cause symptoms due to compression (see CERVICAL
RIB, Vol. III, p. 75).

(g) Articular Malformations

Ankylosis may occur at one or more joints. When many joints are *Ankylosis*
affected the condition is called arthrogryposis multiplex congenita
(γρυπός, crooking or bending). The union is generally fibrous, and the
intervertebral, atlanto-occipital, and mandibular joints generally escape
so that there is free movement of the spine, head, and lower jaws.

Luxation of a joint is often met with, the commonest condition being *Luxation*
congenital dislocation of the hip, the aetiology of which is not known.
The fact that it is six to seven times as common in females as in males
throws doubt upon the explanations of foetal arthritis or foetal com-
pression. It is probably of germinal origin (see also JOINTS, DISEASES
AND DEFORMITIES).

(h) Tumours

Foetal bony tumours are enchondromas and osteomas (see BONE
DISEASES, Vol. II, p. 580). The most interesting are the sacro-coccygeal *Sacro-*
tumours (see Fig. 86), which are differentiated from meningocele and *coccygeal*
dermoid thus: (i) pressure reduces the size of a meningocele; (ii) rectal *tumours*
examination reveals a cleft in the spine in meningocele; (iii) escape
of sebum on puncture indicates a dermoid; (iv) incision reveals the

presence of rudiments of foetal organs and bones in a teratoma. If the tumour is large it may cause dystocia and even rupture of the uterus; in cases in which the infant is born alive the tumour can usually be easily excised. (See COCCYX DISEASES, Vol. III, p. 258, and TUMOURS.)

(3)—Muscles

Diseases of muscles

Myositis

Myositis is possibly the cause of congenital torticollis or wry-neck. Myositis ossificans progressiva may be present at birth and is of unknown aetiology.

Amyotonia congenita

Amyotonia congenita (Oppenheim's disease) may be present at birth and is recognized by flaccidity and loss of power of all muscles, especially those of the lower extremities. The joints are flail-like, and it is easy to flex each hip fully with completely extended knees. Muscular atrophy does not occur, the muscles of deglutition and the sphincters are not affected, and sensation is retained. There is diminution of faradic contraction but not of galvanic, and there is no reaction of degeneration (see ELECTRODIAGNOSIS, Vol. IV, p. 485). The infants are generally well nourished. Treatment is useless and unnecessary. The condition tends to improve spontaneously. It may in later childhood have to be differentiated from Werdnig-Hoffmann's type of progressive muscular atrophy, which is incurable and ultimately fatal. The chief differential diagnostic feature is that the latter is never present at birth, is familial, and consists of weakness as well as atrophy of muscles, starting in the legs and spreading later to the trunk and upper extremities.

FIG. 86.—Congenital sacro-coccygeal tumour

Myotonia congenita

Myotonia congenita (Thomsen's disease), the opposite condition, though congenital, never manifests itself at birth, but may appear very early in life. Cases of congenital hypertrophy of the muscles, accompanied by extrapyramidal motor disturbances and followed by mental deficiency, have been described in new-born infants by Cornelia de Lange, the condition being apparently due to maldevelopment of the corpus striatum.

There may be absence of certain muscles, such as the pectoral muscles, *Malformations of muscles* recognized by the flattening of the anterior chest wall and the prominence of the shoulder-joint (Irvine and Tilley). Other muscles, e.g. the abdominal muscles, are less commonly absent (Housden).

Sprengel's deformity, or congenital elevation of the scapula, is a *Sprengel's deformity* condition in which one or both scapulae are at a higher than normal level owing to unilateral or bilateral absence of the lower part of the trapezius muscle (Middleton). In some cases the scapulae may be attached to the cervical spine by a bar of bone. The deformity is nearly always accompanied by dorsal kyphosis, and in bilateral cases by an apparent shortening of the neck which may have to be differentiated from the Klippel-Feil syndrome (see p. 352). In the absence of bony union, massage, passive movements and gymnastics are sufficient treatment. When bony union is present the condition should be remedied by operation followed by massage and exercises.

Herniae

Diaphragmatic hernia is discussed under the title DIAPHRAGM DISEASES *Diaphragmatic hernia* (Vol. III, p. 677). It may have to be differentiated from a number of conditions, according to the symptom for which the infant is brought *Differential diagnosis* to the doctor. The gastro-intestinal symptoms may simulate intestinal obstruction; the attacks of cyanosis may be mistaken for atelectasis or congenital morbus cordis; the cardiac displacement, in the absence of symptoms, may be mistaken for true dextrocardia or for situs inversus. In cases of doubt X-ray examination settles the diagnosis.

Most of the symptoms and signs of diaphragmatic hernia are also *Eventration of the diaphragm* given by eventration of the diaphragm, i.e. an elevation of one dome of the diaphragm to a much higher level than normal, accompanied by a rise of the underlying viscera. In eventration, however, though the abdominal viscera (e.g. stomach) may appear to lie high up in the thorax —as shown by the X-rays—the dome of the diaphragm is seen to be unbroken. It is probable that, being in many cases symptomless, the condition is discovered only late in life when the person's thorax happens to be X-rayed for a cough or other symptom of obscure origin. When so discovered it may give rise to a suspicion of mediastinal growth compressing the phrenic nerve. I recently had such a case in a woman of 49 years of age. Of the cases discovered in infants some have rightly been attributed to phrenic nerve palsy contracted through injury to the cervical plexus during the delivery of an after-coming head, but the fact that the condition is fifteen times as common on the left side as on the right suggests that most of the cases are true foetal malformations. The presence of 'paradoxical' movement, i.e. rise of the dome in inspiration and fall in expiration should distinguish the paralytic from the congenital type, since in phrenic-nerve paralysis the movement of the affected dome depends entirely upon the intrapleural pressure; during inspiration the negative pressure causes the dome to rise, during expiration the positive intrapleural pressure causes it to

descend. The condition is not amenable to surgical treatment, but electrical stimulation of the phrenic nerve in the neck may be tried.

Other herniae   Other congenital conditions due to failure of certain intratendinous or intermuscular openings to close are inguinal, ventral, and umbilical herniae. These are dealt with in the article on HERNIA.

(4)—Digestive System

Salivary glands

The abnormalities of the salivary glands, such as hereditary absence of the glands, causing dryness of the mouth, calculi, cysts, and tumours are dealt with under the titles PAROTID GLAND DISEASES and SALIVARY GLANDS (SUBLINGUAL AND SUBMAXILLARY) DISEASES. Cloquet recorded that Burdel removed from the sublingual gland of a three weeks' old infant a salivary calculus which was interfering with feeding; the calculus was about the size of a grain of wheat and composed of triple calcium phosphate.

Teeth

Precocious dentition   The only visible dental abnormality in the foetus is precocious dentition, when the infant is born with one or two of the lower incisors erupted from the gums. A few historical persons, e.g. Richard III of England and Louis XIV of France, were born with erupted teeth, and I have met with two cases. If the teeth are loose or interfere with nursing, owing to biting of the nipple, they should be removed, but it must be remembered that they will not be replaced until the permanent teeth come. A case of dicephalic foetus with a full set of teeth in each mouth was recorded by W. T. Rogers (1922).

Other abnormalities   Other dental anomalies only detected by X-rays are: absence of one or more teeth; supernumerary teeth, which may range in number from two to as many as fifty-two, the condition seeming to be a Mendelian dominant. (See also DENTITION, Vol. III, p. 603.)

Tongue

Aglossia   Aglossia or complete absence of the tongue is compatible with life and speech and is due to imperfect development of the first to third visceral arches; it is obviously irremediable and is usually associated with congenital agnathia or micrognathia.

Bifid tongue   Bifid tongue is less rare and can be remedied by freshening the edges of the two halves and suturing the raw surfaces together.

Macroglossia   Macroglossia may be due to increase of interstitial tissue as in mongolism, or to tumour formation, namely, haemangioma and lymphangioma. If the condition is very marked, the mouth cannot be closed, respiration and deglutition may be difficult, and, later on, speech may be interfered with. After dentition the teeth may produce lingual sores, and the protruding tongue may push the teeth horizontally forwards. The condition may be treated by excising a wedge-shaped portion of the tongue.

Microglossia is extremely rare.   *Microglossia*

Ankyloglossia or adherent tongue is a condition in which either the *Ankylo-glossia*
tongue may be firmly attached to the floor of the mouth, needing
operative treatment, or its movements may be only slightly hampered
by a short frenulum. The latter, popularly known as 'tongue-tie', is the
commoner condition, the frenulum being attached too far forwards,
almost to the apex of the tongue. Contrary to popular ideas, the con-
dition does not interfere with sucking which is carried out by mandib-
ular rather than by lingual movements; nor does it render speaking
difficult later on; I have recently seen it in a girl of thirteen, who spoke
perfectly. The condition rarely needs treatment, but, if the mother
insists, it can easily be remedied by gently tearing the frenulum with
the tip of a clean finger. Scissors may cause troublesome bleeding and
should only be used if the finger fails.

In contrast to 'tongue-tie' the frenulum may be too long, allowing the
tongue to fall too far back, with the liability of causing suffocation.
This condition is very rare.

Tumours of the tongue, namely, thyroglossal cysts or cysts at the *Tumours*
foramen caecum, and angiomas are occasionally met with and may,
when present at the base of the tongue, be responsible for unexplained
congenital stridor. The throat should therefore be palpated in all cases
of this condition. (See also GOITRE, p. 629.)

Alimentary canal

Of the numerous abnormalities affecting the alimentary canal the
only ones that need more than a passing reference here are the
following:

Oesophageal stricture may be complete (atresia) or partial. The *Oesophageal atresia*
former is of course incompatible with more than a few days of post-
natal life. In the vast majority of cases it is accompanied by a fistulous
communication between the oesophagus and the trachea. Diagnosis
depends on the observation that the first attempt at swallowing milk
or water is followed by immediate vomiting and attacks of coughing
and choking due to the fluid going into the trachea through the fistula.
Similar symptoms, especially the return of the fluid through the nose, *Diagnosis from cleft palate*
may occur in cleft palate, but the differential diagnosis is readily made
by inspection of the mouth and by the vigorous and voracious sucking
in atresia, as contrasted with the feeble sucking in cleft palate. Cure is
impossible.

Partial oesophageal occlusion is not very rare; as it is not accompanied *Partial stricture*
by a fistulous communication with the trachea, it is compatible with
normal duration of life; it has been recorded in a woman over eighty
years old. It may not be noticed until the child is put on solid food,
when it begins to vomit, and, if the stenosis is very slight, it may not be
noticed at all until discovered in the course of an oesophagoscopy,
X-ray, or post-mortem examination. When the condition is suspected
on account of vomiting, the diagnosis is confirmed, and the site of the

obstruction ascertained, by X-ray examination. The seat of the stenosis is always at the level of the seventh dorsal vertebra. Oesophagoscopy will also decide whether the stenosis is fibrous, as shown by a narrowing of the whole tube, or membranous, of the nature of a diaphragm stretching horizontally across. The latter may be remedied by means of a bougie passed through an oesophagoscope: the former does not as a rule need surgical treatment, attention to diet, which should be fluid or semi-solid, being all that is required. The aetiology of this condition is unknown. It cannot be due to inflammation since the lesion is always situated at the same level. It is probably of germinal origin.

Pyloric and duodenal stenosis   Congenital pyloric stenosis and duodenal stenosis are discussed under the title PYLORUS, OBSTRUCTION.

Stenosis in other sites   Stenosis or atresia in other parts of the bowel may occur and cause intestinal obstruction. The exact
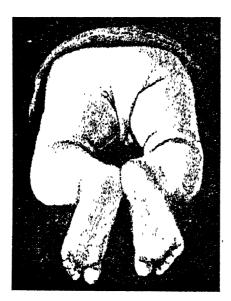
Localization of lesion   site of the lesion is diagnosed from a number of considerations. The longer the interval between ingestion of food and vomiting, the lower the obstruction. Peristalsis in the epigastrium only indicates a lesion high up; peristalsis visible all over the abdomen points to a lesion lower down in the bowel. Rectal examination will exclude imperforate anus or rectum. The cause is not well understood; it may be due to foetal peritonitis, but its tendency to occur in several children of the same parents points to a germinal factor (see p. 345); Findlay met with intestinal

FIG. 87.—Atresia of anus

Treatment   atresia in three consecutive children of the same mother. Treatment is surgical, namely, anastomosis between the portions of the bowel above and below the site of the lesion, unless the atresia is too low, in which case the construction of an artificial anus may have to be considered. Treatment, however, can only be of use if diagnosis is made early and the atresia is not multiple.

Atresia ani   If the anal opening is closed by a membrane (see Fig. 87) the condition can be diagnosed at once and treated by breaking down the membrane with the finger. Generally, however, the occlusion is more extensive, and a plastic operation is needed.

Atresia recti   In atresia of the rectum the anal orifice may be patent but end blindly, the blind end being felt by digital examination. When, however, the atresia is higher up, the condition can only be diagnosed from other intestinal atresias by means of a bougie or by X-ray examination with

an opaque enema. Treatment is immediate operation, if possible before
the onset of symptoms.

In atresia ani-rectalis the occluded portion may communicate with *Atresia ani-*
the bladder, urethra (in the male), or vagina. In such cases there are not *rectalis*
any symptoms of intestinal obstruction, but the passage of meconium
per urethram or per vaginam establishes the diagnosis. The prognosis
is not necessarily grave in the case of ano-vaginal fistula, but is much
graver in the case of ano-vesical fistula, owing to the great risk of
urinary infection.

Hirschsprung's disease is dealt with under the title MEGACOLON: it *Megacolon*
may be present in the foetus although it does not usually come to the
attention of the practitioner before the first year. Meckel's diverti-
culum (persistence of the omphalo-mesenteric duct) is discussed under
the title ABDOMINAL PAIN, Vol. I. p. 1. The appendix may be absent
(see p. 374) or double.

There are various malformations of the bile-ducts, ranging from a *Congenital*
localized occlusion to a complete absence of all the biliary passages. *malformations*
There may also be a double gall-bladder. R. E. Gross gives a com- *of the*
prehensive review of the various types of congenital abnormalities of *bile-ducts*
the gall-bladder, based on a study of 148 cases. Absence of the gall-
bladder or occlusion of the cystic duct does not by itself cause any
symptoms and may remain undetected during life. On the other hand,
occlusion or absence of the hepatic or of the common bile-duct is a
most serious condition.

The pathogenesis of this condition is not clear, and it is not easy to *Aetiology*
explain its preponderance in male infants. The condition cannot be a
true aplasia or lack of development, since both the liver and biliary
passages develop as outgrowths from the duodenum, and there cannot
therefore be a liver without bile-ducts. Rolleston's hypothesis that
maternal toxaemia produces cholangitis leading to occlusion of the
biliary passages could hardly be true in cases in which one of binovular
twins suffered from this malformation but not the other (Feldman and
Lawson; Wallgren; Watkins and Wright). The liver shows considerable
cirrhotic changes, but it is not easy to say whether these are primary
and the biliary occlusion secondary, or vice versa. Syphilis is not a cause.
It is possible that some cases are due to prenatal absorption of toxin,
while others are the result of postnatal toxic absorption from the navel.
To the former class belong those cases in which the jaundice appears at
or very soon after birth, while those cases in which jaundice does not
appear till some time after birth probably belong to the second class.

The commonest condition is atresia of the common bile-duct. It is very *Clinical*
rare, less than 200 cases being on record; it is less rare in male than in *features*
female infants. The baby generally appears normal in every respect at
birth, although it may be slightly jaundiced. If jaundice is present at
birth, the condition may be mistaken for physiological icterus neo-
natorum, until its true character is shown by the change in the stools from
bile-pigmented meconium to clay-coloured faeces, and the appearance

of bile in the urine. If jaundice is absent at birth, nothing wrong may be suspected until jaundice sets in. This happens at any time between the first few days and the first few weeks after birth, most commonly within three weeks, and progressively increases until the skin and conjunctivae become deep yellow. Bile appears in the urine and disappears from the stools. The liver and generally the spleen are enlarged. In the two cases in which I had a van den Bergh test done, one gave a perfect indirect reaction, which is not in conformity with the modern accepted views about jaundice, and the other a diphasic reaction. The nutrition may be surprisingly well maintained for a few weeks, and then the infant begins to waste rapidly and dies from inanition or haemorrhage. The duration of life may be between a few weeks and ten months.

Differential diagnosis   Physiological icterus neonatorum sets in not later than the third or fourth day, is not of the obstructive type (i.e. is not accompanied by coloured urine and clay-coloured stools or by hepatic and splenic enlargement), and tends to clear up in about a fortnight.

Congenital syphilitic jaundice is accompanied by other signs of congenital syphilis and gives a positive Wassermann reaction.

Septic jaundice. In Buhl's disease, leucine and tyrosine crystals are present in the urine; in Winckel's disease the jaundice is accompanied by haemoglobinuria (Feldman, 1927, b). In each of these conditions the jaundice appears soon after birth.

Acholuric family jaundice (see Vol. I, p. 464).

Catarrhal jaundice is exceedingly rare in the new-born and may for a time be indistinguishable from atresia of the bile-ducts. Catarrhal jaundice, however, invariably clears up in a few weeks.

Icterus gravis neonatorum is familial and is accompanied by erythroblastaemia. The jaundice being haemolytic, the urine is acholic and the stools are pigmented. The van den Bergh reaction is indirect (see Vol. I, p. 462).

Treatment   Medical treatment is futile and invariably ends in the death of the infant. If the condition is diagnosed early, before secondary cirrhosis of the liver is far advanced, and pancreatic juice can be removed from the duodenum by means of the duodenal catheter, showing that the pancreatic duct is patent, surgical anastomosis between the gall-bladder and the duodenum, or preferably the stomach, should be considered. If the gall-bladder is absent, anastomosis should be attempted between the bile-duct and the stomach. If the duodenal catheter shows occlusion of the pancreatic duct, or if this condition is found at the operation, any short-circuiting operation is useless, and should not be attempted.

Biliary calculi have been found in still-born foetuses.

(5)—Respiratory System

Nose

Nasal malformations are closures of the anterior and posterior nares —unilateral or bilateral, membranous or bony. Unilateral obstruction may not be noticed at once if it does not sufficiently interfere with respiration. Severe obstruction may interfere not only with breathing

but with sucking. Membranous obstruction may be broken down with a probe; bony obstruction needs more drastic surgical measures.

It should be noted that owing to the normal narrowness of the infant's nasal passages even a normal infant may have difficulty with nasal breathing (snuffles), especially if as a result of intranatal infection there is congestive swelling of the nasal mucosa. Ignorance of this fact may lead to an erroneous diagnosis of syphilitic rhinitis.

In all cases of difficult breathing in a new-born infant, a soft rubber *Diagnosis* catheter lubricated with paraffin should be passed through each nostril. This will detect obstruction and may relieve cyanotic symptoms.

Larynx and trachea

Congenital laryngeal atresia is incompatible with postnatal life. A *Congenital* partial congenital diaphragm of the larynx is sometimes met with and *laryngeal atresia* causes hoarseness and asphyxia. Diagnosis is made with the laryngo-scope, and treatment consists in endolaryngeal division of the membrane. Congenital cysts or tumours of the larynx may occur. Their progressive *Cysts and* growth may completely obstruct the air entry, necessitating immediate *tumours* tracheotomy. Excision of the tumour may then be attempted.

Congenital laryngeal stridor, in which inspiration is accompanied by *Congenital* a high-pitched crowing noise, occurs not uncommonly during the first *laryngeal stridor* week of life. The stridor may be constant or occur only when the infant is excited, being absent during sleep. In the absence of complications, such as rhinitis, laryngitis, or bronchitis, or of tumours at the base of the tongue or glottis, the condition is never serious and tends to dis-appear spontaneously after a few weeks or months; affected children should therefore be guarded from catarrhal processes. The condition may be due to some defective development of the nervous mechanism of respiration or to congenital narrowing of the glottis. It is differ-entiated from laryngismus stridulus by the fact that the latter is a spasmo- *Differential* philic condition which is never present at birth and is accompanied *diagnosis* by other signs of spasmophilia, namely, Chvostek's and Trousseau's signs and changed electrical reactions. It is also differentiated from adenoids and retropharyngeal abscess by the character of the sound and by the fact that these conditions are never present at birth or soon after. The same applies to laryngitis and laryngeal diphtheria. A fatal case of congenital *tracheal* stridor, due to a patent ductus Botalli with the left pulmonary artery constricting the trachea, was recorded by Meyers. (See also ASPHYXIA IN CHILDREN, Vol. II, p. 174.)

Bronchi

Foetal bronchiectasis is rare and cannot be detected clinically unless *Bronchi-* the bronchiectatic area is large enough to form a cyst which shows up *ectasis* in a radiograph. Bronchial atresia is incompatible with postnatal life.   *Atresia*

Lungs

Absence of one lung may exist without any symptoms and be dis-covered accidentally at necropsy. Hernia of the lung through a thoracic

defect is occasionally encountered and is recognized by the presence of an elastic tumour which protrudes through the chest wall and is reducible and resonant on percussion.

Atelectasis   Atelectasis (ἀτελής, incomplete; ἔκτασις, expansion) is a continuation of the physiological foetal state. Complete atelectasis causes the death of the infant immediately after birth. Partial atelectasis produces cyanosis and attacks of asphyxia and must be differentiated from cases of congenital morbus cordis without a bruit, e.g. transposition of the great vessels, and from cases of diaphragmatic hernia or of eventration of the diaphragm due to phrenic nerve palsy. The eventration may indeed be a cause of the atelectasis. Treatment consists in stimulating respiration by administration of a mixture of 93 per cent carbon dioxide and 7 per cent oxygen by means of a special 'sparklet resuscitator' (see Vol. IV, p. 235), and by sprinkling cold water over the baby. During an attack of asphyxia a hypodermic injection of 0·5 c.c. of lobeline hydrochloride and artificial respiration may be needed. (See also LUNG DISEASES.)

Mediastinal cysts

Mediastinal cysts   Mediastinal cysts of gastric or bronchial origin, as well as dermoids, giving rise to cough, dyspnoea, or dysphagia, have been described in infants. Some have been successfully removed, and in one case a spontaneous cure was effected, as shown by X-rays, by the rupture of the cyst into a bronchus (S. G. Schenck and J. L. Stein). See also MEDIASTINUM DISEASES.

Pleura

Hydrothorax   Foetal hydrothorax is rare and, although generally accompanying foetal dropsy (see p. 348), may occur alone. It may cause not only dystocia on account of the thoracic enlargement but also postnatal respiratory difficulty due to pulmonary compression, and has to be treated by paracentesis.

(6)—Heart

Abnormal conditions of the heart are dealt with under the title HEART.

(7)—Genito-Urinary System

Hydronephrosis, cystic kidneys, and renal tumour (all of which may produce dystocia), absence of one or both kidneys, atresia of the ureters or of the male urethra—the latter causing so much distension of the foetal bladder as to hinder birth, 40 pints of urine in the bladder having been reported in one such case (see Fig. 88)—congenital dilatation of the ureters, hypospadias, epispadias, and ectopia vesicae, are dealt with elsewhere (see BLADDER DISEASES; KIDNEY, SURGICAL DISEASES; and UROGENITAL ORGANS, ABNORMALITIES).

(a) In the Male

Anorchia   Anorchia (absence of both testicles) involves incurable sterility. It is of course difficult and sometimes impossible to differentiate the condition from undescended testicles.

Microrchia (small testicles) will also produce sterility due to azoo- *Microrchia* spermia, which may possibly be remedied by injection of anterior pituitary gonadotropic hormones (antuitrin S. or pregnyl).

Cryptorchism, i.e. undescended testicles, if persisting at adolescence, *Cryptorchism* is also a cause of sterility owing to inhibition of spermatogenesis under the raised intra-abdominal temperature. The condition, which till recently was treated surgically, responds well in 33 per cent of cases to treatment by intramuscular injections of anterior pituitary hormone, e.g. pregnyl in 500 rat units twice weekly for six weeks. As spermatogenesis does not begin before the ninth year, treatment should not be undertaken before that age, because the testicles may still descend spontaneously. It should not, however, be postponed too long after the fourteenth year, for if spermatogenesis is inhibited too long the testicle may atrophy. In cases in which treatment by anterior pituitary gonadotropic hormone fails surgical methods should be adopted. (See also TESTIS, UN-DESCENDED.)

For hydrocele see TESTIS, DISEASES.

(b) In the Female

Atresia vulvae generally consists of union of the labia minora. Complete union leads to retention of urine. Incomplete union generally allows escape of urine. The union is usually membranous and can be broken down with a probe. Firmer union needs a plastic operation.

Hydrocele

Atresia vulvae
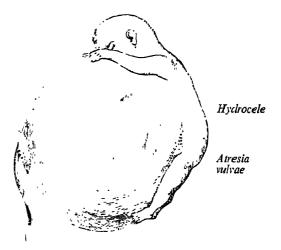
FIG. 88.—Foetus with distended bladder

Atresia hymenalis may be complete or incomplete. The condition is *Atresia* generally not discovered until puberty, when retention of the menstrual *hymenalis* blood occurs, leading to haematocolpos, haematometra, and haematosalpinx in cases of complete occlusion. Incomplete occlusion does not lead to retention of menstrual blood but may form an obstacle to normal marital relationships. As, however, intromission is not necessary for impregnation, pregnancy can occur in such cases. I saw a case in which during labour the hymen, which had an opening no larger than the head of a pin, had to be incised to allow the birth of the foetus.

Ano-vaginal and recto-vaginal fistulae have been described on p. 361. *Fistulae*

To explain the other malformations of the female genitalia some refer- *Embryology* ence to embryology is necessary. The ovaries develop from the genital *of sex organs* glands; the Fallopian tubes from the upper parts of the Müllerian ducts; the uterus and upper part of the vagina from fusion of the lower parts of the Müllerian ducts. Three groups of malformation may therefore occur: (1) Incomplete fusion of the Müllerian ducts producing (i) uterus didelphys, i.e. double uterus and vagina; (ii) uterus bicornis,

i.e. double uterus with one cervix and one vagina; (iii) uterus arcuatus, i.e. a single uterus with a depression at the fundus. (2) Aplasia of the Müllerian ducts resulting in absence of uterus, tubes, and vagina, or absence of uterus and tubes alone. (3) Atresia of vagina alone leading to haematometra and haematosalpinx.

(c) Hermaphroditism

True hermaphroditism

Hermaphroditism may be true or false. True hermaphroditism is the presence of both testicles and ovaries in the same person. Some biologists assign this term to the simultaneous possession of complete sets of both male and female reproductive organs enabling the person to become both father and mother. Such cases have been described, but their authenticity has not been established. Persons with external organs of one sex and genital glands of both sexes undoubtedly occur. Chapple recorded the case of a person whose bodily configuration, external genitalia, and sexual behaviour were feminine, but who at an operation for inguinal hernia was found to have a testicle. In a case recorded by Rutherford a child with the external genitals of a normal boy was found in an operation for inguinal hernia to have a uterus, tubes, and ovo-testes.

True hermaphroditism is embryologically possible because the early embryo possesses the rudiments of both sexes, namely, the Wolffian ducts, which develop into the male organs other than the testes, and the Müllerian ducts, which are the precursors of the female organs other than the ovaries. Both the testes and the ovaries probably develop from the genital gland, the former from the central or medullary portion, the latter from the superficial or cortical portion. Hermaphroditism therefore is a condition in which there is failure of one of the pairs of ducts to atrophy completely.

Pseudo-hermaphroditism

In pseudohermaphroditism, androgyny or gynandry, the external genitals belong partly to one sex and partly to the other sex, but the genital glands are unisexual, testicles or ovaries. Two types exist, masculine and feminine. In the former the external genitals resemble those of a female, because the rudimentary penis is in a state of hypospadias extending to the scrotum, and thus imitates a vulva. When the testicles are undescended, the resemblance to the labia majora is complete. There may even be a vagina of normal length and calibre rendering the person sexually potent as a woman. In such a complete case the sex may never be discovered except for the fact that menstruation never occurs; the sexual characters and libido may be those of a male or of a female (Chapple). Rectal examination would show the absence of a uterus and tubes.

Masculine type

Feminine type

In the feminine type the external genitals resemble those of a male, owing to hypertrophy of the clitoris, which looks like a penis, narrowing or obliteration of the vagina, and partial or complete union of the labia, simulating a scrotum. Prolapse of the ovaries into the labia majora makes the resemblance complete. A case like this was reported

by Rushton Parker (1899). A married 'man' was unable to consummate the marriage, and it was only the periodical monthly discharge of blood per urethram that led to the discovery of the true sex. In another case a 'woman's' true sex was discovered from a laryngological examination for hoarseness, when the vocal cords were found to be of the masculine type (Berthold). Possibly some effeminate men and masculine women belong to these categories, since the secondary sex characters depend on the gonadic hormones.

Generally, however, the appearance of the external genitals of such *Medico-legal importance* children arouses suspicions, and the medical attendant is called upon to settle the sex. This is a matter of great sociological and medico-legal importance. At birth the sex must be registered, and the sex must be known in connexion with legacies and inheritance of titles. The most important problem occurs in connexion with marriage, for, although in many marriages of hermaphrodites normal marital relationships have taken place, in the majority the marriage cannot be consummated. I saw a 'widow' who had lived happily with her husband for a number of years: her vagina was a cul-de-sac about one inch long. Rectal examination revealed the absence of a uterus.

When the sex cannot be settled without a laparotomy—which may *Bringing up of herm-aphrodites* not be practicable—the child should be reared as a boy because: (i) The 3:1 ratio of the male to the female type renders such a procedure more likely to be correct. (ii) Should the child turn out to be a female, the true sex will probably show itself at puberty with the onset of menstruation. If, however, it is reared as a girl when it is really a boy, the true sex may not be discovered till long after puberty, and constant association with girls (e.g. at a boarding school) may, as has happened, result in unpleasant complications. (iii) The chances of contracting a homosexual marriage are greater if the child is brought up as a girl. Blair Bell's advice to rear the child in accordance with the greatest resemblance of external genitalia to the male or the female sex seems therefore to be unsound.

In view of recent work in connexion with the detection and quantitative *Biochemical diagnosis* estimation of the sex hormones in the urine, oestrone in the female and androsterone in the male, it should in the near future be possible to settle the sex of a hermaphrodite by biochemical means.

Hermaphroditism may occur in several children of the same parents, *Aetiology* and the father of an hermaphrodite is frequently himself a hypospadiac —but not an hermaphrodite, because such a person is probably always sterile. Broster and Vines have demonstrated in the cortical cytoplasm of the adrenals of an hermaphrodite the same fuchsinophil cells as they discovered in the cortical hyperplasia associated with adolescent virilism in women. These cells secrete a masculinizing hormone—not, however, identical with the ordinary male hormone, androsterone— which can be detected in, and isolated from, the urine in cases of virilism. After unilateral adrenalectomy this adrenal hormone is diminished in the urine of such patients. Further, the fuchsinophil cells

are normally present for about seven or eight weeks during the early foetal life (9th to 17th weeks), in the adrenals of both male and female foetuses, but appear earlier, are more abundant, and disappear later in the male than in the female foetus. Broster and Vines (1933 and 1937), therefore, attribute hermaphroditism to a failure of this adrenal androgenic hormone to disappear in the female foetus at the time when the Wolffian ducts are due to atrophy, and believe that the degree of masculinization depends upon the duration and intensity of this hormone in the female foetus. The 25 per cent incidence of the female type of hermaphroditism they explain on the assumption of the presence in the male foetus of an as yet undiscovered feminizing hormone.

Treatment Once the sex has been established the appearance of the external genitalia can be restored by plastic operation as well as—in the case of a female hermaphrodite—by amputation of the hypertrophied clitoris. It also seems to follow logically that if the androgenic hormone is found in an infant hermaphrodite, unilateral adrenalectomy to diminish the hypersecretion would be a correct procedure. This would be specially indicated if a tumour of the adrenal were found by palpation or by a pyelogram showing downward displacement of a kidney.

(8)—Endocrine System

Thyroid
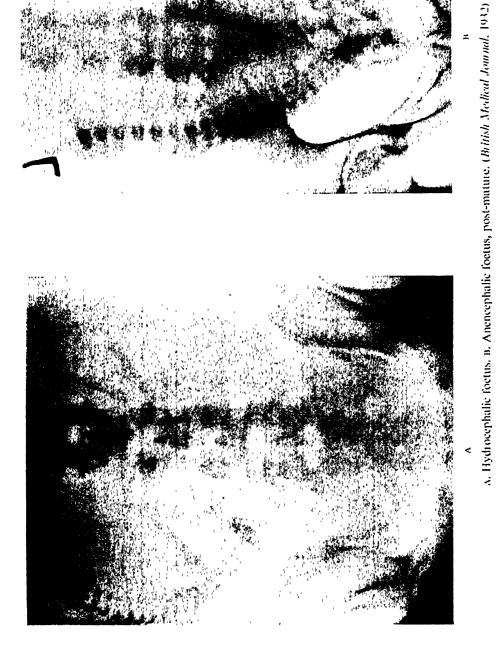
Tumours Thyroid enlargements, for example teratomas, may, by their size or by their causing extension of the foetal head, bring about considerable dystocia. Congenital goitres are fairly common in goitrous regions and usually occur in foetuses of goitrous mothers. Nevertheless it would appear that the condition is not hereditary but due to the lack of iodine in the water and food in goitrous districts. When the supply of iodine is scanty, not only may the mother suffer but she will not have enough to transmit to her foetus. Treatment is mainly prophylactic. In goitrous areas the expectant mother should be given potassium iodide to use as table salt. Infants born with such enlargements should not be left alone in their cots unwatched, as sudden flexion of the head during sleep may cause fatal asphyxia. (See also CRETINISM, Vol. III, p. 489, and GOITRE AND OTHER DISEASES OF THE THYROID GLAND, p. 599.)

Myxoedema Congenital myxoedema in the new-born is extremely rare, because, even if the thyroid is atrophied or absent at birth, the foetus has probably received enough thyroid secretion from the mother through the placenta to guard it against hypothyroidism until some time after birth. Nevertheless cases are occasionally recognized by the typical appearances and are treated by the administration of thyroid. (See also MYXOEDEMA.)

Exophthalmic goitre A typical case of foetal exophthalmic goitre, due to placental transmission of excessive thyroxin from a mother suffering from the same disease, was recorded by Clifford White in 1912.

A. Hydrocephalic foetus. B. Anencephalic foetus, post-mature. (*British Medical Journal*, 1932)

PLATE IV

Thymus

Enlargement of the thymus is important from two points of view, *Enlarge-* namely, sudden death soon after birth due to 'status lymphaticus', and *ment* the suggestion put forward by some that congenital laryngeal stridor is caused by thymic enlargement. Absence of the thymus is sometimes *Absence* associated with anencephaly.

Adrenals

Absence of the adrenals or of their boundary zone (foetal cortex) is *Absence of* almost constant in anencephaly. But the fact that in such monsters the *cortex* adrenal medulla may be normally developed proves that the cerebral hypoplasia is not due to defective foetal cerebral circulation, the result of low blood-pressure brought about by absence or deficiency of adrenaline. Moreover, the fact that in anencephalic monsters of less than five months' foetal age the boundary zone with its fuchsinophil substance is normally developed shows that the adrenal cortex is not responsible for anencephaly. Indeed, it has been shown that the anterior lobe of the pituitary produces an adrenotropic hormone which controls the growth of the adrenal cortex (since cortical hypoplasia follows hypophysectomy in rats), and it is therefore probable that both the anencephaly and the adrenal cortical hypoplasia are the result of failure of development of the pituitary. The cause of the latter is not clear. The presence of anencephaly in one only of mono-amniotic (uniovular) twins excludes pressure of a small amniotic sac but not necessarily some germinal condition as the cause of the monstrosity (see p. 370).

Haemorrhage into the adrenals of the new-born may cause sudden death (see ADRENAL GLAND DISEASES, Vol. I, p. 244).

(9)—Nervous System

Hydrocephalus is dealt with under the title HYDROCEPHALUS. Here it *Hydro-* may be mentioned that foetal hydrocephalus, if at all large (cases have *cephalus* been known in which the circumference of the head was about 30 inches and the amount of contained fluid was 20 pints), may produce very serious dystocia with rupture of the uterus. The condition can be detected before birth by abdominal palpation and X-rays (see Plate IV). In such cases Caesarean section should never be considered (unless it is necessary for legal purposes to have a child born alive), since the foetus, if born alive, inevitably grows up as a crippled imbecile. In head presentations the fontanelle should be incised to evacuate all the fluid and the head crushed with the cephalotribe. In breech presentations the spinal canal should be opened and a catheter passed right up into the cranial cavity to ensure complete evacuation of the fluid, even in the obstructive type (when the foramen of Monro is closed) when mere lumbar puncture would not suffice.

Anencephaly or congenital absence of the cerebral hemispheres and *Anencephaly* of the cranial vault occurs about once in 2,000 births, is about three

times as common in female as in male foetuses and tends to be familial. Although sometimes associated with amniotic adhesions at the cranium, it is often found without them; therefore the adhesions are not an aetiological factor. It is also not due to prenatal rupture of a hydrocephalus, because the base of the anencephalic skull is usually convex, instead of concave as it should be if anencephaly had been preceded by hydrocephalus. Moreover, its frequent association with extensive spina bifida and malformations of other organs which cannot have any aetiological relation with either adhesions or hydrocephalus rules out these conditions as causes.

The association of anencephaly with adrenal hypoplasia was discussed above (p. 369). Probably both conditions are primarily of germinal origin, since they may occur in several sibs as well as in twins. Anencephaly would therefore seem to be a Mendelian recessive character (see p. 345). On the other hand, Litt and Strauss recently published a case of mono-amniotic (uniovular) twins, of which one was normal and the other anencephalic. This case can be explained on the supposition that on complete separation of the blastomeres, after the first segmentation of a fertilized ovum of the genetic constitution Aa ('A' representing dominant normality and 'a' recessive anencephaly), disintegration of the A-gene occurred in one of them. The blastomere containing an a-gene uncontrolled by an A-gene would develop into an anencephalic foetus, whereas the other containing both A- and a-genes would give rise to a normal foetus of the genetical constitution Aa (Dr. E. A. Cockayne in a personal communication).

Antenatal diagnosis   Hydramnios is present in about 75 per cent of the cases, and, in the absence of twins, should arouse suspicion of anencephaly if the woman has previously produced such a monster. X-ray examination decides the diagnosis (see Plate IV). The foetus generally presents by the face and, the flat head not being a good dilator of the cervix, difficulty may occur with the birth of the shoulders.

Treatment is impossible, and postnatal life does not as a rule continue for longer than a few days. In view of the tendency of the condition to recur in sibs, parents who have produced such a monster should abstain from further reproduction.

Porencephaly   Porencephaly, i.e. flattening of the brain due to cystic degeneration, and giving rise to symptoms of cerebral diplegia, may be familial. Der Brucke has recently recorded the condition in two successive infants born to a mother with hare-lip and cleft-palate. The infants usually die soon after birth.

Hernia of the brain is a protrusion of some part of the intracranial contents through an opening in the skull, generally at the junction of some of the cranial bones, and corresponds to the protrusion of some part of the spinal cord in spina bifida. It is obviously due to failure of the primary cerebral vesicles to close, but the cause of such failure is not at all clear. The suggestion that it is due to a hypersecretion of cerebrospinal fluid is supported by the fact that hydrocephalus may

co-exist with. or may follow. the successful cure of cerebral hernia or
of spina bifida. The fact that as a rule radical cure of these anomalies
is not followed by hydrocephalus may be explained on the supposition
that there is a tendency for the rate of secretion to slow down to normal
—a phenomenon sometimes seen in the treatment of the non-obstructive
type of hydrocephalus by repeated lumbar puncture. This hypothesis,
however. does not explain why the hypersecretion should lead in some
cases to hydrocephalus. in others to cerebral hernia: in others again to
spina bifida at various levels. and in still others to a combination of
two or more of these abnormalities. It is probable that some cases are
caused by amniotic adhesions pulling upon the rudimentary brain.

Hernia cerebri occurs about once in 4.000 births, and appears in the *Sites and*
middle line of the skull or a little to the side of it. in the following *frequency*
situations:

Occipital (73 per cent). in the region of the external occipital pro- *Occipital*
tuberance either above or below the tentorium. The superior occipital
variety may communicate with the posterior fontanelle. whereas the
inferior occipital may come through the foramen magnum when it is
indistinguishable from cervical spina bifida. In fact the two conditions
may co-exist.

Frontal or sincipital (17 per cent). There are three subvarieties of this: *Frontal or*
(i) naso-frontal, the hernia appearing at the base of the nose. between *sincipital*
the frontal and nasal bones; (ii) naso-orbital. at the inner angle of the
orbit, between the frontal. ethmoid, and lacrimal bones; and (iii) naso-
ethmoidal, protruding between the bony and cartilaginous portions
of the nose. The naso-orbital is the rarest of these subvarieties.

Basal (10 per cent). These appear inside the nasal cavity (intranasal), *Basal*
by passing through the lamina cribrosa of the ethmoid—a position to
be remembered by the rhinologist operating on intranasal tumour—
or in the pharynx, and even hanging outside the mouth by protruding
through the junction between the sphenoid and ethmoid bones.

Lateral (very rare), in the region of the postero-lateral foramen.   *Lateral*

Cerebral hernias are of the following three types: (i) Meningocele, *Types*
consisting of a sac of the dura and arachnoid, containing subarachnoid
cerebrospinal fluid, but no brain tissue. (ii) Encephalocele, containing
in addition some brain tissue. (iii) Hydrencephalocele or encephalo-
cystocele, when the herniated brain tissue contains cerebrospinal fluid
which communicates with a lateral ventricle. The brain tissue may be
greatly thinned out by the pressure of the enclosed fluid.

Cerebral hernias vary in size from that of a walnut to that of the foetal *Size*
head and may cause dystocia.

The symptoms depend upon the size, situation, and type of the hernia. *Symptoms*
A small occipital, naso-frontal, or naso-ethmoidal hernia may not cause
any symptoms. On the other hand a naso-orbital hernia, even if small,
may compress and displace the eyeball, and the intranasal and
pharyngeal varieties of basal hernia may cause nasal obstruction or
dysphagia respectively. A large hydrencephalocele may cause spastic

paralysis. optic atrophy, and subsequent idiocy. If the skin over it is thin. it may ulcerate and lead either to rupture and escape of a large amount of cerebrospinal fluid, or to death from septic meningitis.

Physical sign: meningocele
A meningocele is smooth, pedunculated, symmetrical (spherical or pyriform) and. because it is filled with fluid, translucent on transillumination. Also. because the fluid communicates with the subarachnoid space. the swelling can generally be seen to pulsate synchronously with the heart-beat and to become tense when the infant cries. If, however, the pedicle is very narrow, such pulsation may not be perceptible. Digital pressure pushes the fluid back into the intracranial subarachnoid space, producing bulging of the fontanelle as well as symptoms of cerebral irritation (crying, twitching, or convulsions), or of compression (rigidity, drowsiness. dilatation of the pupils. and slowing of the pulse). Further digital pressure may produce Cheyne-Stokes respiration and even death. The swelling is partly or completely reducible.

Encephalocele
An encephalocele is usually small, smooth. and symmetrical, but is generally not pedunculated. It usually pulsates, but, because the layer of subarachnoid fluid is so thin, does not fluctuate and is not translucent to transmitted light. Digital pressure may, however, cause bulging of the fontanelle as well as symptoms of cerebral irritation. It may or may not be reducible, according as the opening through which it protrudes is large or small. Encephalography shows the presence of brain tissue.

Hydr-encephalocele
A hydrencephalocele is large, irregular, and pedunculated. Its degree of translucency depends on the thickness of the brain tissue layer. It fluctuates, but as there is practically no subarachnoid cerebrospinal fluid between the membranes and the brain substance this hernia does not pulsate and pressure does not cause bulging of the fontanelle or symptoms of cerebral irritation or compression. Ventriculography will demonstrate the communication between the hernia and the lateral ventricle.

Diagnosis from caput succedaneum and membranes
Intranatally, a cerebral hernia may be mistaken for caput succedaneum and the presenting membranes. A caput succedaneum pits on pressure, whereas a hernia cerebri does not. Fluid displaced by the finger from the membranes returns immediately; fluid displaced from a hernia takes a little time to return.

Postnatally, the following swellings must be excluded: (i) Caput succedaneum pits on pressure and does not possess that combination of signs characteristic of any one type of cerebral hernia, since it does not fluctuate. does not pulsate, does not when pressed cause bulging of the fontanelle or symptoms of cerebral irritation, and is opaque on transillumination. Moreover, a caput succedaneum begins to diminish in size almost immediately and disappears altogether in a few days.

From cephal-haematoma
(ii) Cephalhaematoma is not present at birth but develops later, and then gradually diminishes in size and disappears in a few weeks. Also, being an effusion of blood under the periosteum. it is limited by the sutures and therefore lies over one bone only, usually one of the parietals. It fluctuates, is not translucent, does not pulsate, and when pressed does

not cause bulging of the fontanelle or symptoms of cerebral irritation. (iii) A lipoma may be present at birth in the positions occupied by cerebral hernias, but it does not possess the combination of signs characteristic of any type. *From lipoma*

Intranatally, if a hernia causes obstruction it must be punctured to allow the escape of cerebrospinal fluid, when the foetus can be delivered naturally or instrumentally. Postnatally, except in the case of very small meningoceles which may sometimes undergo a natural cure as the result of the gradual absorption of the contained fluid and the obliteration of the lumen of the pedicle by the union of the suture round it, treatment is always surgical. Ernest Sachs condemns treatment by the injection of sclerosing fluids. Compression is equally of no avail and may be dangerous. A meningocele the pedicle of which is not too wide may be tied off. *Treatment: hernia*

A small encephalocele may as a rule be excised and the defect closed by a metal plate, or by a transplant from the infant itself or from its mother. If the portion of brain removed belongs to the 'silent area', no ill results will follow. In the case of a large encephalocele, despite the small chances of success, operation should be undertaken, as without operation the outlook is practically hopeless. A hydrencephalocele is inoperable and should be left alone. *Encephalocele* *Hydrencephalocele*

Out of 50 cases of all types of hernia of the brain that have been operated on 41 recovered, whereas in the majority of unoperated cases —with the exception of small meningoceles which sometimes undergo a spontaneous cure, or may remain stationary without causing any trouble for many years—death occurs within a few days from septic meningitis following infection due to ulceration of the skin. *Prognosis*

The most favourable cases for operation are those with narrow pedicles and those which are most accessible, e.g. the frontal and superior occipital. Contra-indications are: (i) the presence of other deformities which are likely to lead to early death; (ii) the presence of hydrocephalus or of microcephalus; (iii) an encephalocele of the inferior occipital type which extends through the foramen magnum; and (iv) a large hydrencephalocele. *Indications and contra-indications for operation*

Other foetal diseases of the nervous system are: spastic diplegia (Little's disease) not due to cortical intranatal trauma but to imperfect development of the cortical motor areas and the pyramidal tracts (see CEREBRAL DIPLEGIA, Vol. III, p. 27); congenital nuclear palsies due to imperfect development of the nuclei of some of the cranial nerves, such as the third (congenital ptosis) or the third, fourth, and sixth (complete ophthalmoplegia externa); and foetal meningitis. *Little's disease* *Congenital nuclear palsies* *Meningitis*

It is extremely difficult to differentiate between spastic diplegia of intranatal origin and that of developmental germinal origin, but the bilateral distribution distinguishes the congenital nuclear from the traumatic 'birth' palsies. Another diagnostic point is the rapid recovery in peripheral obstetric palsies, such as facial paralysis. *Differential diagnosis of diplegias*

(10)—Sense Organs

Eyes

For congenital abnormalities of the eyes see BLINDNESS, Vol. II, p. 410.

Ears

Among the abnormalities are malformations. absence of various constituent portions. and supernumerary auricles (see DEAF-MUTISM, Vol. III. p. 552).

Other Malformations

Other malformations are discussed in the articles on the organs concerned.

(11)—Situs Inversus

Situs inversus or complete visceral transposition (see Fig. 89) does not affect the health of the person, except that it is often accompanied

FIG. 89.—Radiograph of situs inversus
(Proceedings of the Royal Society of Medicine, 1935)

by other congenital abnormalities. Thus, a girl aged twelve years had no appendix, and another, a baby three weeks old, had some congenital abnormality of the cardiac auricles, as shown by an abnormal P wave

in its electrocardiogram (Feldman, 1925; 1935). Haas (quoted by Tow) found at autopsy absence of the gall-bladder and bile-ducts in a case of situs inversus. The condition often remains undetected and is a Mendelian recessive character (see p. 345).

7.–MALFORMATIONS IN RELATION TO FOETAL PHYSIOLOGY

509.] Many malformed foetuses, such as those with anencephaly, intestinal atresias, urethral atresia, absence of both kidneys, or absence of both lungs, are born alive and fully grown and yet cannot survive birth; this proves that foetal existence depends entirely upon the placental interchange of material between mother and foetus. That complete oesophageal atresia is consistent with good foetal nutrition shows that the foetus does not derive any nourishment from the liquor amnii. The absence of oligohydramnios in cases of absence of the kidneys and ureters (Gowar) or of urethral occlusion shows that this fluid is not entirely derived from foetal urine. The fact that the foetuses of hyperglycaemic mothers are fatter than normal shows the part played by carbohydrates in the formation of foetal fat. The absence of the adrenals, or, at any rate, of the adrenal cortex, in anencephalic foetuses shows that there is some relation between these endocrine glands and the development of the brain. The various vital activities temporarily shown by anencephalic infants, such as respiration, cardiac action, sucking, defaecation and micturition, prove that these functions do not originate in the cerebral hemispheres and must therefore be of reflex origin. Lastly, the occurrence of hermaphroditism, in which the foetus possesses some of the organs of each sex, shows that, although sex is normally determined by the chromosome constitution of the fertilizing spermatozoon, this gametic influence may in certain circumstances and in varying degrees be overcome. The phenomenon of freemartinism in the cow clearly shows how this is effected in cattle. A freemartin is a cow-calf which is the binovular co-twin of a bull-calf. It is always sterile and has the internal genitals of a bull, and occurs only in the binovular bovine twins in which a free blood circulation between the two twins allows the testicular hormone of the male to be passed over and to masculinize the female co-twin. This mode of masculinization, however, does not occur in man, because although intercommunication is common between the circulations of uniovular twins, leading very rarely to the production of an acardiacus and fairly frequently to the death of one of the twins (see p. 346), such circulatory interchange probably never occurs in human binovular twins. The factor which disturbs the mechanism of the sex chromosome in human hermaphroditism is endocrinological (p. 367); and the fact that the condition tends to be familial suggests that the primary cause of the abnormal endocrine constitution may lie in another chromosome.

8.–DOUBLE MONSTERS

510.] Double monsters, i.e. two foetuses joined together, occur on the average only about once in 50,000 births, but they are of enormous interest to the embryologist, the anatomist, the physiologist, the psychologist, the obstetrician, the surgeon, and the sociologist.

(1)—Embryology

Origin of double monsters

Their origin has been explained in three different ways: (i) That they arise from an ovum fertilized by two spermatozoa. This view is untenable, since experiment shows that such eggs disintegrate immediately after the entry of the second spermatozoon. (ii) That they originate from the fusion of two separately fertilized eggs. This is theoretically possible because double monsters have been experimentally produced in aquatic eggs in this way; but that human conjoined twins do not generally arise in this manner is certain, because not only would the components be expected to be sometimes of opposite sexes, which has never yet been authentically found in human pathology (law of homosexuality), although it sometimes occurs in cattle, but such an occurrence should on statistical grounds be twice as common as their being either both males or both females. For the following events are equally probable: (*a*) both males; (*b*) both females; (*c*) first child male, second child female; (*d*) first child female, second child male. So that there are two sets of unlike sex to each pair of males or females. (iii) The only possibility therefore left is that they represent the incomplete separation of blastomeres during the early stages of segmentation of a single fertilized ovum, and that they are in fact incompletely separated uniovular or homologous twins. Experimentally, double monsters have been produced in this way, by incompletely separating the blastomeres in aquatic eggs either mechanically or by alternating the temperature, chemical composition, or oxygen content of the medium in which they were developed. Several facts favour this view. First, the components of all human conjoined twins so far authentically recorded in the literature are of the same sex. Secondly, the junction invariably occurs between anatomically similar structures, such as skull with skull, pelvis with pelvis, sternum with sternum, or liver with liver (St. Hilaire's law of affinity of like for like). This can only be explained on the hypothesis of incomplete blastomere separation, since on that of coalescence there is no reason why one part of one developing egg, such as the head, should not unite with any other part of the other egg, such as the pelvis, thorax, or abdomen. Thirdly, Bertillon's statistics show conjoined twins to be most frequent in places such as Savoy, where uniovular twinning is commonest, but not among Magyar women, who hold the record for binovular or fraternal twins (Lesbre).

There are, however, a number of facts which do not quite fit in with this explanation: (i) Female conjoined twins are two or three times

commoner than male, instead of being about equally common as should be and indeed is the case with identical twins. (ii) Though comparatively common in certain animals, conjoined twins do not, as far as I know, occur in the armadillo, which always bears sets of uniovular quadruplets. (iii) Though both the law of homosexuality and the law of St. Hilaire (the latter with the exception mentioned on p. 379) apparently hold good in human conjoined twins, they are not invariably true in other mammals, in which several authentic cases have been recorded of conjoined twins of opposite sexes, as well as of union occurring between heterologous parts. It has been suggested that even human conjoined twins may be of opposite sexes, but no indisputable case has been published. In a personal communication (1937) Dr. Ellen Kent Hughes of Armidale, New South Wales, stated that ten years ago, in the presence of two other doctors, she delivered a woman of a still-born six months' double monster (thoracopagus) of which one foetus was male and the other female. The specimen was not preserved. Moreover, as will be seen later, unlike what is the case in separated uniovular twins, the components of a conjoined pair differ from each other considerably in facial appearance, anthropometric measurements, intelligence quotients, and psychological outlook. Even their finger-prints show greater differences than appear in identical twins (Reichle; Cummins and Mairs), although I am not aware of any observations made regarding their blood groups. Lastly, Sangvichien recorded a case in which hare-lip and cleft-palate were present in one of the components only. Thus the blastomere-splitting hypothesis, though probable, does not satisfy all the facts.

Genetically it is interesting that, although conjoined twins are commonest in districts where uniovular twinning is most frequent and are often born to parents of whom one or other may be a twin or belong to a family in which twinning is common, such twinning in the family is generally of the binovular or fraternal type. The mother of the Siamese twins Eng and Chang had binovular twins several times. Moreover, none of the children of conjoined twins (and the conjoined brothers Chang-Eng are said to have had between them 22 children) has ever been either a separated or a conjoined twin. Even in the case of animals in which it is possible to arrange for both parents to be conjoined twins the offspring have so far always been normal, showing that the condition is neither a dominant nor a recessive Mendelian character. *Genetic considerations*

Anatomically, conjoined twins are interesting from the point of view of their internal and external modes of union. Omitting any description of their internal anatomy, brief reference will now be made to the mode in which they are externally united, because it forms a basis for their classification. (For description of anatomy see Mudaliar.)

(2)—Classification

Double monsters may be classified into:

A. Completely symmetrical conjoined twins or cosmobia (κόσμος, order; βίος, life), or diplopagi (διπλόος, double; πάγος, union), in which each *Double autosites*

component is a perfectly complete independent individual, so that, if the two were surgically separated, each could live apart from the other. Each such component is called an autosite (αὐτός, self; σῖτος, food), i.e. self-supporting. They are therefore also called double autosites and may live for many years.

B. Incompletely symmetrical conjoined twins in which only certain parts of the body, such as the head and neck or the pelvis and legs, are duplicated. These are generally born dead or die soon after birth.

Auto-parasites

C. Asymmetrical conjoined twins, when one of the two bodies is not fully developed and lives as a parasite on its completely developed partner, the autosite, so that when surgically separated the autosite could continue to live but not the parasite. They are therefore called auto-parasites and may live for many years.

Anadidyma

Double monsters may therefore be divided into: (a) Anadidyma (ἀνά, up; δίδυμος, twin), when the doubling is from the head downwards, resulting (in the most complete specimen) in a psodyma (ψόα, loin; δίδυμος, twin), i.e. a monster in which there are two heads and trunks but only one pelvis and one pair of legs. Dicephalic monsters belong to this group.

Katadidyma

(b) Katadidyma (κατά, down), when the splitting is from below upwards, resulting (in the most complete specimen) in a monster consisting of one head, two trunks, two pelves, and two pairs of legs. These two groups generally cause dystocia because of the extensive and immobile

Anakata-didyma

union. (c) Anakatadidyma, when the fission is both from above downwards and from below upwards. All the live double autosites, such as the Siamese twins, the Bohemian sisters, and the Brighton twins (Violet-Daisy Hilton), belong to this group and, owing to the slightness and mobility of their union, offer as a rule no obstetric difficulty. When the fission in anakatadidyma is absolutely complete, the result is a pair of homologous, identical, or uniovular twins. With complete fission but unequal development of the foetuses the heart of the stronger foetus overcomes that of the weaker, which may die and shrink up into a

Auto-parasites

shapeless acardiac monster. (d) Auto-parasites.

Nomenclature of double autosites

Classification of anakata-didyma

The generic name for double autosites is pagus, which means union. This term is prefixed by another Greek word indicating the site of the union. Thus thoracopagus, the commonest type, constituting some 65 per cent of all human double monsters, means one in which the bodies

Thoracopagus

are united at the thorax, such as the sternum (sternopagus) or the xiphoid cartilage (xiphopagus). In the latter there is only a band-like union consisting of skin, cartilage, blood-vessels, and a portion of liver. The Siamese twins Chang-Eng Bunker, the sisters Radica-Doodica, and others were xiphopagous. A case of thoracopagus in tubal pregnancy was

Pygopagus

recorded by Mosettig. Maria-Rosalina was sternopagous. Pygopagus is a double autosite in which union is at the pelvis (πυγή, buttocks), most commonly at the sacrum and coccyx, so that the bodies of the cosmobia are placed back to back. Although rarer than thoracopagus

it is not very uncommon, several having occurred in recent years, e.g. the Blazek sisters Rosa-Josepha, and Daisy-Violet Hilton (the *Brighton* Brighton twins). One of the sisters of the Brighton twins was *twins* married in Texas in 1936 at the age of 27, and four years before the twins were cited as co-respondents in a successful divorce suit. A variety of this group, however, ischiopagus (union at the ischium), in which the long axes of the two bodies are practically in the same straight line, is very rare. Such cosmobia are either born dead or die in early infancy. Craniopagi may be par-   *Craniopagus* ietal, occipital, or frontal, according to the bones between which the union occurs. Some craniopagi have lived as long as ten years. Very rarely there may be a cranio-pagus occipito-frontalis, in which the frontal bone of one foetus is united with the occipital bone of the other, the long axes of the two bodies being in the same straight line. This variety is the only ex-ception to St. Hilaire's law of affinity of like for like in human pathology (see p. 376) and is difficult to reconcile with the accepted blastomere-splitting hypothesis of the origin of double monsters. In both craniopagus occipito-frontalis and ischio-pagus, the two bodies lying as they do in the same straight line, there is as a rule no difficulty with their birth.

Nomenclature of incompletely symmetrical conjoined twins

Cephalo - thoracopagus means union   *Cephalo-*
between the heads and thoraces of the   *thoraco-*
foetuses. If such a union produces a   *pagus*
monster with two faces (see Fig. 90), the   FIG. 90.—Diprosopus distomus
monster is called diprosopus (πρόσωπον,   tetrophthalmus diotus with
face) or Janus (after the double-headed god   hydrocephalus and hare-lip
of Roman mythology). Dicephalus is a monster with two separate *Dicephalus* heads. If such a monster also has two separate necks, it is a diceph-alus diauchenus (αὐχήν, neck). If it has only one neck, it is a dicephalus monauchenus. Dipygus is one with a doubling of only the *Dipygus* lower parts of the body, namely pelvis and legs. There are a few other types which are not of sufficient interest to be enumerated here.

Nomenclature of auto-parasites

Auto-parasites may be divided into:

(a) Heteropagi (ἕτερος, other), in which a perfectly distinct but small *Heteropagi* and incomplete twin—the parasite—is attached to the autosite in a manner similar to that in which the double autosites are united.

Heteralians   (b) Heteralians (ἅλως, disc), in which the parasite consists of some portion or portions of another foetus, such as head, head and thorax, or lower part of the body, attached to the autosite. A monster with an accessory inverted head attached to the top of the autosite's head is a craniopagus parasiticus or epicomus (ἐπί, upon; κόμη, hair). Such a monster, which lived for a few years, was first described by Everard Home in 1790. If the parasite consists of the upper part of the body attached to the thorax of the autosite, the monster is a thoracopagus parasiticus or heterodymus, e.g. Colloredo of Genoa of the 17th century, who is said to have been the father of several children, all normal. If the lower part of the parasite is attached to the autosite, the monster is an epigastrius, or heteradelphus (ἀδελφός, brother), e.g. the Hindu boy Laloo, and the Chinese boy A-Ke. In one case described by Buxtorff the monster was the father of four children, all normal.

Polygnathians   (c) Polygnathians (γνάθος, jaw), in which the parasite springs as a shapeless mass from the maxilla of the autosite—epi- and hypognathus, in which the mass is attached to the upper or lower jaws respectively.

FIG. 91.—Endocyme foetus found enclosed in cyst in abdomen of boy. When removed it was as rosy and as healthy as if alive. The specimen is preserved in the Teratological Collection at the Royal College of Surgeons. (*British Medical Journal*, 1929)

Polymelians   (d) Polymelians, in which the parasite consists of one or more limbs attached to the pelvis of the autosite.

Endocymians   (e) Endocymians (ἔνδον, within; κῦμα, foetus), in which the parasite is enclosed within a certain part of the foetus, i.e. the parasite is an included foetus. Sacro-coccygeal teratomas (p. 355) and epignathus are examples, but the most striking case is that of an almost complete foetus inside the abdomen of another foetus (foetus in foetu). A specimen of such a foetus removed from the abdomen of a boy ('extra-uterine pregnancy in a male') is in the Museum of the Royal College of Surgeons of London (see Fig. 91).

(3)—Physiology
Double autosites

Viability   If double monsters are regarded as part of a series, at one end of which are the separate homologous twins and at the other end the teratomas,

such as sacro-coccygeal tumours, then those which approximate to one or other end of this series have the best chance to live the normal span of life. Hence with double autosites the best prognosis belongs to xiphopagi and pygopagi in whom the union is very slight, i.e. when there is very little admixture of organs, and with auto-parasites the autosite has the greatest chance of survival when the parasite is a teratoma that can easily be removed, and when the parasite is not in such a position as mechanically to interfere with the vital processes of the autosite, as happens, for instance, with an epignathus which interferes with the autosite's respiration and feeding.

In respect of other physiological and psychological processes, the two components may be considered as two distinct and separate entities, and, apart from being of the same sex, differ from each other more than homologous twins. They differ in looks, height, girth of chest, and cephalic and other anthropometric measurements. *Resemblances between components*

Their heart-beats are not synchronous; their pulse-rates, blood-pressures, character of the sphygmograms, and blood counts are different even in health, and these differences are accentuated when one of the two autosites is taken ill. *Circulation*

The respirations are not synchronous and differ in frequency as well as in depth, so that the vital capacities are different. *Respiration*

Their muscular forces as measured by the dynamometer, their reaction times, and their sensitivity to pressure, are different, except at the site of union. Their reflexes are generally independent. One autosite cannot control the movements of the other; their thoughts and tastes are different and their dreams are different. There is no transference of thought between them, and their differences of opinion may even lead to blows. For instance, in the case of the Siamese twins, Chang-Eng Bunker, one was an alcoholic and the other a total abstainer, and of the Bohemian Blazek sisters, Rosa became a mother, while Josepha was sexually frigid. Moreover, during Rosa's pregnancy, Josepha continued to menstruate up to about eight weeks before the confinement, showing an absence of pituitary hormone interchange between them; on the other hand after the confinement both of them secreted milk and each was able to nurse the child. The two components may be carrying on different conversations at the same time; one may be awake while the other is asleep, and they may feel hungry and respond to the calls of nature at different times. One may have diarrhoea and the other constipation. Micturition and defaecation, however, depend upon their internal anatomical connexions. *Neuro-muscular system* *Psychology* *Hormones*

Their mode of progression depends upon their external union. If they can both face forwards, as the xiphopagi, they both walk in the same direction; otherwise they walk sideways, or one walks backwards while the other walks forwards, as the sternopagi, or some pygopagi. *Mode of progression*

Their dermatoglyphics (i.e. palm, sole, and finger prints) are different, as are also their intelligence quotients. I am not aware of any observations made on the blood groups of conjoined twins, but on the blasto- *Dermatoglyphics*

mere fission hypothesis the two components should always belong to
the same group. It is said that in some cases situs inversus exists in one
of the components, but the statement has not been recently confirmed.
Borchers described a case of situs inversus in the parasitic part of a dead
double monster but did not state if the position of the viscera in the
autosite was normal. It may be contended that situs inversus might be
present in one only of the members of conjoined twins as a result of
'mirror-image' development. But if this were the case we should expect
the condition to be present in one of the co-twins of all double monsters
as well as of all separated identical twins. If such a finding is sub-
stantiated, it would, as situs inversus is a Mendelian recessive character,
be important evidence against the uniovular origin of such twins, since
the visceral transposition would be expected to be present in both or
in neither. If, however, they have the same malformation, it appears
in one as the mirror image of the other. Thus, hare-lip will be on the
right lip of one and on the left lip of the other. An illustration is given
by Courtright and Austin. (But see Sangvichien's case, p. 377.)

(4)—Pathology

One may be ill without affecting the other. Thus, Josepha but not
Rosa had diphtheria at the age of fourteen, and Rosa but not Josepha
was operated on for vesical calculus at the age of thirty-two. Of the
Radica-Doodica xiphopagus, Doodica but not Radica suffered from
tuberculous peritonitis. The fact that, notwithstanding the intercom-
munication between the two circulations, as shown by experiments
with diffusible substances such as sodium salicylate and methylene blue
(when one of the drugs ingested by the one component appeared in
the urine of each), the temperature of the unaffected twin was normal
in spite of the pyrexia of the other, suggests that pyrexia is not neces-
sarily due to changes in the blood. In the case of the pygopagi Lucio
and Simplicio Godino in whom there was also a communication be-
tween the two circulations, Lucio contracted pneumonia without
Death   infecting Simplicio (see p. 384). The death of one is quickly followed by
that of the other.

Auto-parasites

For the physiology and pathology of auto-parasites special mono-
graphs must be consulted, such as those of Ernst Schwalbe (1907) and
Hübner. The latter contains a bibliography of nearly 1,100 references.

(5)—Obstetrics

Obstetrically, double monsters are of obvious interest. Contrary to
expectation, many of them are born spontaneously without any help
from the accoucheur. According to Hohl, in 73 out of 119 cases, i.e.
60 per cent, delivery was natural, and 29 sets were born alive. There
were four maternal deaths in the whole series, i.e. about 4 per cent, due
to rupture of the uterus. The favourable termination is due to the small-

A

B

Antenatal diagnosis of double monster, cephalo-thoracopagus. A. The radiograph shows single head at pelvic brim, two spines united at base of skull, and four pairs of limbs. B. The same after birth. (Mr D. W. Currie's case)

PLATE V

ness of foetuses, as is the case with ordinary twins, as well as to the mobility of their union in the case of anakatadidyma.

Antenatal diagnosis is practically impossible without X-ray examina- *Diagnosis* tion. In the gross abnormalities in which there is only one foetal heart suspicion is aroused by feeling two heads or other homologous parts without hearing more than one foetal heart. Even X-ray examination fails to diagnose most of the conjoined twins, in which the union is cartilaginous, from ordinary twins. Plate V shows a case of cephalo-thoracopagus diagnosed antenatally by radiological examination. The recently introduced amniography, i.e. X-ray examination of the uterine contents after aspiration of some liquor amnii and injection of abrodil into the amniotic cavity. may prove to be a useful diagnostic method, because by rendering the liquor amnii radio-opaque it shows up the foetal soft parts; but the method is still in its experimental stage. In any case, routine X-ray examination at about the seventh month would detect the grosser abnormalities, and induction of premature labour would save the mother. Intranatal diagnosis is made when the expulsion of the foetus is arrested.

(6)—Surgery

The question of separating double monsters may arise in three different circumstances; as an expediency, as an urgency, and as an imperative necessity. When the two autosites are perfectly healthy and well formed and their union is not very extensive or complicated, separation is expedient in order to render each independent. Although in most cases their guardian's or their own consent is unobtainable, because of the large fortunes made by such abnormalities as objects of curiosity at travelling fairs, nevertheless separation has been effected in a number of cases, mostly xiphopagi. The first case in which both children survived the operation was the one separated by Fatius of Basle in 1689. *Separation* The only other successful separations with survival of both children *at birth* described since then are those recently effected by D. W. McLaren of Nigeria, and by H. H. Holm. Among others it is interesting to note that Böhm in 1861 separated his own babies (female xiphopagus) im-mediately after birth, which took place spontaneously 2 to 3 weeks prematurely; one died four days later, and the other lived for five years. Separation is urgently called for when one of the autosites is smitten with a chronic incurable disease. Doyen of Paris in 1902 separated the Indian xiphopagus, Radica-Doodica, when at the age of twelve Doodica developed active tuberculosis; Doodica died a few days after the operation, but Radica lived and improved in health. In the case of the Blazek pygopagus, Rosa-Josepha, Breakstone of Chicago offered to separate them when Josepha was taken seriously ill, but permission was refused by their brother. A case of imperative necessity was published by Rudolf Jolly in 1905. A female xiphopagus, of which one was alive and the other still-born, was operated on by Olshausen. The live child died forty-three hours after the operation. Another such case

was recorded in the daily press in Nov. 1936. Lucio and Simplicio Godino were pygopagous twins twenty-eight years old who married two sisters. Soon after Lucio's death from pneumonia, Simplicio was separated from his dead brother.

Now that the thermo-cautery has considerably obviated the risk of haemorrhage in division of the hepatic union, surgical separation of conjoined twins should be comparatively simple, especially if radiography fails to reveal any extensive bony union or any union between their intestinal tracts.

In the case of auto-parasites similar indications prevail.

(7)—Sociology and Medical Jurisprudence

Monsters in medical jurisprudence   No matter how serious the degree of monstrosity, there is no legal excuse for ending the life of a child after it has been completely born, and any person committing such an act is guilty of murder. It is, however, right and proper to destroy such a monster intra partum, if it produces dystocia as it generally does. So long as, but not unless, a monster born in wedlock has human shape, it may in English law, as laid down by Blackstone, be an heir. A mother, therefore, who dies during labour, is succeeded by the monster, even if it is incapable of surviving for any length of time. The mother's estate goes to the monster's relations and not to her own.

At birth the question of registration of a double monster as a single infant or two infants arises. The Brighton female pygopagi, recorded by Rooth in 1911, which were born to a mother who was herself a twin, were registered as separate births, and the Public Vaccinator charged a double fee for vaccinating them, although it is probable that one vaccination might have sufficed for the two. The Blazek pygopagi were compelled by Law to take two railway tickets when travelling. Also, when both of them died intestate, Rosa's son claimed the estate left by the unmarried Josepha, while the other relatives claimed part of the estate left by Rosa. Further, when female conjoined twins have a common vagina, the question of marriage of one of them might raise an interesting problem, because the husband might be prosecuted for bigamy. Another difficult problem might arise in the case of a criminal offence committed by one of the twins. Are both of them to be sent to prison, although physiological considerations have shown them to be separate persons? An interesting anecdote is related in Talmudic literature. A dicephalic monster is said to have claimed a double portion of his dead father's estate. King Solomon ordered hot water to be poured on one of the heads, when the other head joined in the cry of pain; Solomon therefore ruled that the monster was a single individual and dismissed his claim.

9.—TRIPLE MONSTERS

511.] These are too rare to justify description here. Three such cases have been recorded during the present century.

10.—PREVENTION OF MORBID FOETAL CONDITIONS

512.] The prevention of foetal exanthemata has already been considered under the various microbic diseases. It consists in isolating the mother from contact with cases of infectious disease or from carriers. In addition, every woman who might be syphilitic should have a Wassermann test done, and, if it is positive, she should have efficient antisyphilitic treatment. During an epidemic of smallpox the mother's vaccination will protect her unborn infant, provided the vaccination is done not too late after her exposure to the disease. Malaria is prevented by efficient treatment of the mother with quinine or atebrin.

As regards the prevention of malformations and monstrosities, a good deal can be done by eugenic measures, since many such malformations are known to behave as Mendelian dominants or recessives. In addition, in view of the teratogenic effects of X-rays or radium, no woman should be exposed to such radiations during the very early weeks of pregnancy. Indeed, some go so far as to say that, if such a woman has unwittingly been exposed to large doses of these radiations, it is justifiable to induce abortion. The influence of alcohol and lead has already been discussed on pages 341 and 342.

No method is known of preventing double monsters; but, in view of the experimental evidence to the effect that alteration in intra-uterine temperature or oxygen may produce such monsters, it is necessary to protect the mother during the earliest days of pregnancy from pyrexial or asphyxial conditions, although there has so far been no clinical evidence of an association between maternal pyrexial and circulatory diseases and double monsters.

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FOOD

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DIET IN TREATMENT   METABOLISM
DIETETIC DEFICIENCY   METABOLISM, BASAL
  DISEASES   VITAMINS
INFANT FEEDING

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1.–MAJOR CONSTITUENTS OF FOOD

513.] Strictly speaking, the term food should include not only the more solid portions of the diet and liquids such as milk, which contain large amounts of nutritive material, but also water, which is in some respects the most important food of all and without which life cannot be maintained for more than eight or ten days.

In spite of its varied appearance, texture, and flavour, food consists

essentially of water, nitrogenous constituents, fats, and carbohydrates, combined together in different proportions and associated with some fifteen mineral elements and certain organic compounds termed vitamins, which are required in only relatively small amounts and differ considerably among themselves in constitution and properties.

(1)—Water

Nearly all food contains water. There is about 40 per cent in bread, 70 per cent in flesh foods, 5 to 50 per cent in nuts, and 85 to 95 per cent in vegetables and fruits. Water is also formed from the organic part of the food during its metabolism and oxidation, but, in spite of this, man invariably supplements his food by drinking additional water. About 2,500 c.c. are lost daily from the lungs and skin and in the urine and faeces, and this must all have entered through the mouth, but the supply is as a rule so generous and natural regulation so perfect, that water as a constituent of food need not be further discussed.

(2)—Nitrogenous Constituents

The nitrogenous constituents are mainly the proteins, but many *Nitrogenous* other nitrogen-containing compounds have been isolated from foods *constituents* of all kinds, and it would be incorrect to suppose that the whole of the nitrogen in any food was present as protein. Flesh foods, for example, contain purines, extractives, and urea, all of which are nitrogenous, but none of which are proteins. Most of the nitrogen in mushrooms is urea, which has no dietetic importance. The proteins consist of amino-acids linked together, and each amino-acid may be regarded as a unit in the protein molecule.

Plants can synthesize all the amino-acids that they require from inorganic materials. Animals can, to a large extent, change one amino-acid into another, but they cannot build them up from inorganic materials; they therefore depend for their existence on a sufficient supply of protein in their food. About six amino-acids cannot be manufactured by mammals and have to be taken as such in the food.

The main sources of protein are animal foods, including not only flesh *Proteins in* foods of all kinds but also eggs, milk, and cheese. Milk and all animal *plant and* foods are considered to be of special value dietetically, for their proteins *animal foods* contain all the amino-acids required for human nutrition. In the usual edible plants proteins are present in smaller amounts than in foods of animal origin. Further, plant proteins may contain inadequate amounts of some of the essential amino-acids. Apart from cereals, nuts, and legumes, plant foods contain so little protein that, as sources of this constituent, they may almost be neglected in a consideration of human dietaries.

In addition to nitrogen, the proteins in the food constitute the body's *Sulphur* main source of sulphur, for almost the whole of this element is ingested in the form of cystine or methionine, which are two of the amino-acids commonly present in the protein molecule. All proteins are not equally

good sources of these two amino-acids, but on a mixed diet this is not important.

(3)—Fats

Fats have a high fuel value. Each molecule of a simple fat consists of glycerol united to three fatty acids. Cholesterol and other sterol esters are also found in small quantities both in plants and animals.

Sources of fat   Fat may be derived from animal or vegetable sources. Butter, lard, dripping, suet, and fat of meat are typical animal fats. Cheese, eggs, and some fish also contain quite large amounts. Some kinds of margarine and most frying oils are prepared from vegetable sources, mainly from nuts and seeds, but olive oil is also of great commercial importance. Speaking generally, however, fruits and vegetables are a poor source of fat and contribute little or none to the average mixed diet.

(4)—Carbohydrates

Carbohydrates may be divided into two main classes: (i) the soluble sugars, and (ii) their more complex and less soluble condensation products such as starch and cellulose.

Sources of carbohydrate   Animal foods, with the exception of milk, contain practically no carbohydrate. Generally speaking, plant foods are our main source of supply, and 90 per cent of our carbohydrate is derived from starch, eaten in the form of cereals or potatoes, and from sugar, a product of the sugar-beet or sugar-cane, which is used for flavouring and other purposes.

2.–CALORIFIC VALUE OF FOOD

Calories   514.] The fuel value of food is measured in Calories. A Calorie is defined as the amount of heat required to raise the temperature of 1 litre of water through 1° C. It has been found by experiment that the combustion of 1 gram of carbohydrate or of protein in the body provides 4·1 Calories, whereas the combustion of 1 gram of fat gives 9·3 Calories. It is therefore clear that different foods will have different calorific values according to the proportions of protein, fat, and carbohydrate in them. The following list shows the comparative calorific values of some common foodstuffs. Each portion will give 100 Calories, so that the smaller the weight the higher the calorific value of that particular food:

Butter – – – – – –	½ ounce
Bacon, fried – – – – –	⅗ ounce
Chocolate – – – – –	⅘ ounce
Sugar – – – – – –	⅞ ounce
Bread – – – – – –	1½ ounce
Beef, roast – – – – –	1½ ounce
Eggs – – – – – –	1½ eggs
Potatoes, boiled – – – –	4 ounces

Milk	–	–	–	–	– 5 ounces
Apples	–	–	–	–	– 9 ounces
Tomatoes	–	–	–	–	– 20 ounces
Cabbage	–	–	–	–	– 50 ounces

3.–INORGANIC SALTS

515.] In the human body there are at least fifteen mineral elements, and each one is essential for life. About one-twentieth of the body-weight consists of mineral matter; since inorganic salts are lost from the body daily through the kidneys and skin and in the faeces, these losses must be made good from the food. The more important inorganic essentials are *Essential* sodium, potassium, calcium, magnesium, iron, copper, manganese, zinc, *minerals* chlorine, bromine, iodine, and phosphorus.

From the dietetic point of view, the minerals which require most consideration are those of which there is likely to be a shortage. These are mainly calcium, phosphorus, iron, and iodine. If the diet provides for these in adequate amounts, the others can usually be left to look after themselves.

The amount of each mineral present in different foods varies a great deal. A food which is a rich source of one element is often a poor source of another. Milk, for instance, is rich in calcium and phosphorus but poor in iron.

An abundant supply of calcium and phosphorus is needed whenever *Calcium* active bone-growth is taking place, but many foods which are highly nutritious in other ways contain very little calcium; bacon, butter, and bread are good examples. Foods rich in calcium are cheese, milk, eggs, green-leaf vegetables, and nuts. The most important single source in this country is undoubtedly milk, and a milkless diet is usually a very low calcium diet.

Flesh foods of all kinds, milk, eggs, and cheese contain abundant *Phosphorus* supplies of phosphorus. Plant foods on the other hand, with the exception of whole cereals, nuts, and legumes, are a relatively poor source of this element. Since, however, most people of British extraction include flesh foods or dairy products in their diets, it is probable that their food generally contains enough phosphorus for their needs.

The main sources of iron are liver, eggs, brown bread, meat, and green *Iron* vegetables. Milk contains very little, but Nature has to some extent overcome this deficiency by arranging that the foetus should be born with enough iron in its body to meet its requirements over the suckling period.

Copper, like iron, is stored by the foetal liver, the new-born infant *Copper* bringing a sufficient supply into the world to last it till the milk period is over. The element is necessary for life, but as all foods contain small amounts there is no practical fear of a copper deficiency in diets which are otherwise adequate.

Minute amounts of iodine are needed for normal nutrition. Part of the *Iodine*

iodine is used for the synthesis of the hormone thyroxine, which plays such an important part in the regulation of metabolism. Iodine may have other functions. It has been shown that in areas where goitre is endemic the intake of iodine is low, and, further, that the addition of iodine to the water-supplies may be a most important therapeutic measure. The chief sources of iodine are probably the sea, the soil, and drinking-water. Vegetables, especially those grown near the sea, and all fish and seaweeds contain iodine. The sea contains considerable amounts, but in the manufacture of table salt the iodine is refined away, so that ordinary table salt contains none.

Sodium and chlorine   Sodium and chlorine may be considered together. There is enough sodium in the milk for the growing baby. In temperate climates a man can live on flesh foods without added salt. Plant foods, on the other hand, contain much less sodium than animal foods and relatively more potassium. The amount of potassium in a fruit or vegetable may be a hundred times the amount of sodium, and only the merest traces of chlorine may be present.

With the introduction of agriculture thousands of years ago the change in the dietetic habits of the people brought trouble in its train. Our forefathers began to suffer from a shortage of salt and developed a craving for it. Additional salt became a necessity of life, and in very early times it acquired not only commercial but also religious significance. At the present time most of our sodium and chlorine is obtained from salt which has been deliberately added to food to improve its flavour or act as a preservative.

Potassium   Potassium is the predominating base of all cellular tissues, whether animal or vegetable. It is unnecessary to consider it in human diets, because there is no fear of a deficiency, and an excess is easily removed through the kidneys.

Magnesium   Magnesium is one of the essential elements, and comparatively large amounts of it are required. When young animals are totally deprived of it, lesions of the blood-vessels and nervous system soon appear, and chronic shortage leads to defective bones and teeth. Human deficiencies need not be anticipated, for all foods contain salts of magnesium, and they are readily absorbed.

Zinc   Zinc is present in all tissues and may be essential to life. All foods contain traces, and milk contains more zinc than iron, copper, or manganese.

Cobalt   Cobalt appears to be necessary for the correct nutrition of sheep and probably other mammals and man, but nothing is known of its function.

Manganese   Manganese is also indispensable, but small amounts only are necessary, and an excess may be very toxic.

Bromine   Bromine in foods has been little investigated, but its constant presence in the blood and tissues and its variations in disease suggest that it has a function.

Other metals   Traces of rubidium, aluminium, silver, arsenic, tin, and lead are constantly found in living tissues and may or may not have important functions. They are derived entirely from food and drinking-water.

4.–VITAMINS

516.] Very little is known about the quantitative distribution of vitamins in food, because their estimation presents considerable difficulty. Chemical methods are available for the determination of vitamins A and C, but the others can only be estimated biologically. (See also DIETETIC DEFICIENCY DISEASES, Vol. IV, p. 56, and VITAMINS.)

Vitamin A (fat-soluble) Vitamin A is required by everyone, especially children, for normal growth and health. It is a fat-soluble substance which gives a specific colour reaction with antimony trichloride. It is related to carotene, a pigmented and unsaturated hydrocarbon. As the body can convert carotene into vitamin A, therapeutically the two can be considered together. *Sources* Liver, butter, cream, spinach, carrots, dried whole milk, and cheese are excellent sources of vitamin A, and a great many other common foods contain appreciable amounts. There is not a great loss during ordinary cooking, so that clinical deficiency of vitamin A is not likely to be common.

Signs of deficiency Experimentally, young animals deprived of vitamin A ultimately cease to grow and develop night-blindness and xerophthalmia, a non-specific infection of the lacrimal glands and conjunctival sac. In addition to the ophthalmia, infections of the mucous membranes of the alimentary, respiratory, and urinary tracts have been shown to be exceedingly prevalent in animals deprived of vitamin A. Lesions of the central nervous system can also be produced, and female animals fail to ovulate. The infections are not of any one pathological type, and the organisms which gain a footing owing to the weakened resistance of the mucosa are of the type commonly found there in small numbers during health. Night-blindness was recognized clinically at the time of Hippocrates, and even then eating liver was the traditional cure. Xerophthalmia has been recognized clinically in Vienna, Denmark, and Japan, and, very rarely, in Britain. Genuine clinical deficiency undoubtedly has been met with but only on very unbalanced diets, which would not have been countenanced for a moment by any authority.

Vitamins B_1 and B_2 (water-soluble) Vitamin B_1 protects from beri-beri. Vitamin B_2 may be one of the factors which prevent pellagra. The distribution of the B vitamins in nature is wide, and they are not easily destroyed by cooking. Eggs are a potent source, wholemeal bread, also yeast and its autolysed extracts such as marmite. Vegetables, fruit, milk, and animal organs all contain good supplies and meat lesser but still appreciable amounts. There is not yet absolute proof that a shortage of the B vitamins commonly occurs in this country, although suggestions are now frequently made that it may.

Vitamin C (water-soluble) Vitamin C, or ascorbic acid, is closely related in chemical structure to the hexoses. Scurvy develops if there is not enough vitamin C in the diet, and minor deficiencies are thought by some to be relatively common. Vitamin C occurs naturally in fresh fruit and vegetables, and the

Sources amount present varies very much according to the species. The best sources are oranges, lemons, tomatoes, grape-fruit, and raw green vegetables. Bananas also contain a moderate amount. Grapes, on the other hand, contain almost none, and some varieties of apples are very poor sources. Potatoes contain moderate amounts, and it is probable that a large number of human beings depend almost entirely upon potatoes for their supply of vitamin C.

Vitamin C is partially or wholly destroyed by cooking, especially in the presence of soda or other alkali; commercial canning also leads to a considerable degree of destruction, though if the canning is carried out in the absence of air the loss of vitamin C is partially prevented. In potatoes and tomatoes vitamin C appears to be more stable to heat than in most other fruits and vegetables. Pasteurization of milk destroys about half its vitamin C.

Vitamin D
(fat-soluble) A number of sterols and sterol derivatives possess antirachitic activity. Some occur naturally, and several can be prepared from inactive sterols by the action of ultra-violet light. Vitamin D is probably the most important vitamin in Great Britain, since it is the one which is most likely to be grossly deficient. Very few foods are good sources of this vitamin, and children may require more than they can obtain from a mixed diet if they are to develop perfect bones and teeth. Vitamin D is found in egg yolk, summer butter, cream, and milk, and fat fish such as the herring. Halibut- and cod-liver oil are rich sources. Lard and other pig fats are deficient in this vitamin, and plant fats contain none.

Other
vitamins Vitamin E and other vitamins are discussed under the title VITAMINS.

5.–THE AVAILABILITY OF CERTAIN FOOD CONSTITUENTS

517.] The availability of food is a subject which has been coming to the
Definition of
'available' fore in recent years. To be available, food must be absorbed and utilized, but 'available' has not quite the same meaning as 'digestible'. Some complex carbohydrates, for example, may be broken down in the intestine and the products absorbed. They are therefore digestible, but if soluble sugars are not formed and absorbed, they are not available as a source of carbohydrate to the body. Simple mineral salts, to which the term indigestible cannot be applied, may be unavailable if they are in some form which cannot be absorbed.

Available
carbohydrate The old method of determining the amount of carbohydrate in a foodstuff was to calculate it 'by difference'. Everything which was not water, protein, fat, or ash was reckoned as carbohydrate. This carbohydrate fraction contained a complicated medley of substances. These were mostly carbohydrates in the strict chemical sense of the term, it is true, but many of them were not carbohydrates so far as the animal was concerned. Thus fibre, cellulose, and all the complicated pentosans and hexosans which make up the cell walls of plants were calculated as

carbohydrates and given a food value equal to that of starch and the sugars. This led to considerable errors in computing diets, for many green vegetables contain very little starch and sugar but considerable amounts of pentosans and cellulose. These last substances are not attacked by any of the digestive enzymes. Any decomposition they may undergo is bacterial in origin and takes place mainly in the large intestine. Although, moreover, they consist of sugar molecules closely linked together, the products of the bacterial disintegration are carbon dioxide, hydrogen, methane, and fatty acids. They cannot therefore be considered as sources of sugar to the human body. Some vegetables, notably artichokes, contain 10 to 20 per cent of inulin, a fructose condensation product which is not attacked by the digestive enzymes. It may therefore be regarded as unavailable and should be discounted in making up a diet. The methods used at the present time for the determination of carbohydrate in foodstuffs differentiate the readily available sugars and starch from the unavailable mixtures of carbohydrates which are mainly valuable as 'roughage'. The starch and all the individual sugars are separately determined, and the sum of these constitutes the available carbohydrate.

For some years past interest in the anaemias and iron therapy has been *Available iron* keen, and one of the problems often raised has been that of the absorption of iron from the intestine. No one has ever questioned that elements such as sodium, potassium, and chlorine are freely absorbed, but iron is rather different. In the first place, iron tends to form insoluble salts, particularly phosphates, which would only be absorbed with difficulty. In the second place, iron is present in food in two forms, inorganic and organic. The latter consists of the blood iron, haematin iron from muscular tissues, and compounds of the same type which are widespread in nature and act as respiratory catalysts. Popular opinion would certainly have accorded to this organic iron a high degree of nutritive value. When the matter was put to the test, however, it was found that organic iron was of very little value in nutrition. As judged by its power to promote haemoglobin regeneration, inorganic iron was found to be much more effective than organic, the reason being that iron cannot be absorbed in the organic form. Pepsin and trypsin, moreover, only liberate iron very slowly from the haematin molecule. It has been estimated that not more than 5 per cent of such iron would be set free during ordinary digestion, although more than this can be set free *in vitro* by prolonged enzyme digestion. Such being the case, it is clear that in considering the iron content of foods the important matter is not so much their total iron as the proportion of this which is in available form.

A study has recently been completed of the amounts of inorganic iron *Sources of* in most of the common foodstuffs eaten in Great Britain. In some all the *inorganic iron* iron seems to be in the ionizable inorganic state, but in others only a small percentage of it. Thus, little of the iron in meat, but nearly all the iron in liver, eggs, white fish, and cereals is available. Most vegetables and many fruits fall into an intermediate category, but some fruits and

nuts have a very high percentage of their iron in available form. It follows that meat, in spite of all the iron that it contains, may be a poor source of the metal, and eggs and brown bread are really far better. In contradistinction to iron, copper in food is thought to be entirely in an available form.

Available calcium and phosphorus Like iron, calcium tends to form insoluble salts, and it is due to this fact that so much of the food calcium may at times pass through the alimentary canal without being absorbed. Excess of inorganic phosphates in the diet may bring this about, especially if the stomach juices are not acid. The masses of fatty acids passing through the intestine unabsorbed in sprue and coeliac disease bind calcium as the insoluble soaps and prevent its absorption. The calcium in spinach is said to be quite unavailable because of the excess of oxalic acid present in this plant.

In just the same way that inorganic phosphorus can prevent the absorption of calcium by the formation of insoluble salts, so calcium, iron, and other metallic radicals can prevent the absorption of phosphorus. Beryllium does this most effectively and in consequence causes severe rickets when its salts are added to an animal's diet.

In some foods, however, both phosphorus and calcium may be unavailable, because they are present in organic combination. Whole cereals, nuts, and legumes, for example, contain inositol hexaphosphoric acid, generally in the form of an insoluble double salt of calcium and magnesium. This insoluble compound is usually known by the trade name 'phytin'; 50 to 80 per cent of the total phosphorus in cereals and nuts may be in this form. At one time this organic phosphorus was thought to be of great value, but it has been shown that such phosphorus is largely unavailable. Further, if inositol hexaphosphate is not hydrolysed in the intestine, it may hold large amounts of calcium in the intestine as the insoluble salt and so prevent its absorption. In this way phytin phosphorus, by being itself unavailable, may render calcium unavailable also.

6.–FOOD REQUIREMENTS AND INTAKES

518.] It is unfortunately true that, in spite of all the work done up to the present, our quantitative knowledge of human food requirements is largely based upon assumptions which have no experimental foundation whatever. It is necessary first of all to define what is meant by re-*Minimum and optimum requirements* quirements. It would appear that the term can be used in two senses, minimum requirement and optimum requirement. The minimum requirement for the correct nutrition of adults may be defined as the least amount of any dietary constituent necessary to maintain a perfectly healthy person in equilibrium for a given period of time. Optimum requirements for adults may be stated to be the minimum requirements for perfect health, plus an additional allowance for unforeseen eventualities. Actually, very little is known about the minimum requirements

of the various dietary constituents and still less about the optimum requirements.

In considering food requirements, dietary constituents may be conveniently divided into two classes: (i) those of which too much is just as harmful as too little, e.g. calories and possibly vitamin D; (ii) those which are readily excreted, so that an excess is not in any way harmful and may in fact be beneficial. Theoretically, there is not any true optimum for these dietary constituents. Calcium and potassium are good examples.

The actual food intakes of men have been studied to some extent, but usually on groups of persons, and very little is known about the personal variations. The food intakes of women and children have rarely been studied. Intakes, however, are not synonymous with requirements and should never be so regarded, so that these measurements afford little guide as to either the minimum or optimum requirements for health.

There is much divergence of opinion among different authorities about the human protein requirements. It is known that a certain minimum is *Organic constituents* required to maintain nitrogen equilibrium, but it is probable that above this minimum considerable variations in protein intake are compatible with health. In Europe and America the average protein intake among men is 70 to 100 grams a day, i.e. 1 to 1·4 gram per kilogram of bodyweight. Women as a rule eat less protein than men, but there is little difference if their lower body-weight is taken into consideration. Children are generally considered to require more protein per kilogram of body-weight than adults, because their metabolism is more active and provision must be made for growth as well as for maintenance; 2 to 2·5 grams per kilogram are generally considered to be ample.

Fat and carbohydrate intakes show still wider variation. Carbohydrate in the form of cereals and potatoes is the cheapest form of nourishment in many countries, and the poorer classes tend to subsist largely on this type of food. As incomes rise the proportion of fat in the diet increases, while that of carbohydrate decreases. In a recent investigation it was found that English middle-class men were eating an average of 130 grams of fat and 350 grams of carbohydrate a day. A small group of unemployed studied at the same time were eating 95 grams of fat and 397 grams of carbohydrate. These variations do not approach the variations in the diets of nations as a whole. Some Eastern nations and many of the agricultural people of southern Africa eat very little fat; the latter may eat only some 5 to 15 grams per day. They derive almost all their nourishment from carbohydrate. The Eskimos, on the other hand, do not eat carbohydrate food to any extent and lead healthy lives. It is, therefore, absurd to lay down any rules about the requirements of fat or of carbohydrate.

A man's food intake in European and American countries is generally reckoned to provide about 3,000 Calories per day. People show considerable variations, but these are small compared with the variable relations possible between carbohydrates and fat. The extremes in 63

Englishmen's diets were 1,772 and 4,955. Women tended to eat less than men, not only per person but also per kilogram of body-weight, and their intake expressed on this basis decreased with advancing age.

Inorganic elements   The human requirements for the inorganic dietary constituents are not known. Several suggestions have been put forward about the allowances which should be made for men, women, and children of various ages, but these are largely empirical and are not based on experimental evidence.

Calcium   A recent investigation showed that the average daily intake of calcium among English middle-class men was about 0·9 gram per day. Women's intakes averaged 0·63 gram. Some individuals ate very much less than this, but there is nothing to suggest that these peoples were not getting enough calcium for their immediate requirements. Pregnant or lactating women, however, and growing children would certainly require more.

Phosphorus   The average intake of phosphorus among the same group of middle-class men was 1·6 gram a day and 1·1 gram among women. This was almost all in an available form. There is not any reason to suppose that these intakes are inadequate, but to state that they are men's and women's optimum requirements, or that they bear any relation to their optimum requirements, would be an unwarranted assumption. It is most important to realize this, for at the present time there is a tendency to investigate the intakes of groups of people and to refer them to standards set up arbitrarily in other countries, which are accepted without question as 'requirements'.

Iron   The average intake of iron among men is of the order of 15 to 16 mgm. a day, very much less than that of calcium or phosphorus but probably enough for their requirements. In England women's intakes were found to be lower and to average 11·4 mgm. a day. This was due to the fact that women ate less food and also tended to eat less meat, which is a rich source of iron, although much of the iron is probably not available. There is good reason to believe that this intake is not enough for adult women's physiological requirements, for their haemoglobin levels are about 10 per cent lower than those of men and can be raised almost to the men's level by the administration of iron. Young children of six months to three years and pregnant women suffer very commonly from an iron deficiency. It is probably true to say that half the population in Great Britain would benefit from an increased iron intake.

Iodine   Iodine is one of the minerals which are essential for life, but only in the most minute quantities. The average man's daily intake is only some 15 millionths of a gram a day.

Vitamins   Our knowledge of the chemistry of vitamins and food is not yet far enough advanced to enable us to assess either the intakes or requirements of vitamins in man from a study of the food. Nevertheless, tests have been evolved in recent years which claim to indicate whether the intakes of some of the vitamins are adequate or not. It is as though we had no knowledge of the amount of iron in food and so could make no statement of the normal human intake, but by estimating the haemo-

globin in the blood we could readily detect deficiency. Thus, tests for a person's powers of light and dark adaptation seem to reveal latent vitamin A deficiency. Vitamins B_1 and C can be determined in the urine and the results used to assess the adequacy of the vitamin intake. Deficiency can be confirmed by noting the response to a feeding test. It should be possible before long to state vitamin intakes and requirements in terms of units, or even of milligrams a day, but for the present we must rest content with being able to detect minor degrees of deficiency.

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FOOD POISONING

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Reference may also be made to the following titles:

1.–DEFINITION

519.] Food poisoning may be described in general terms as any illness due to the ingestion of unwholesome food or drink. It includes therefore such diverse conditions as poisoning by inorganic chemicals, such as lead, arsenic, and antimony; by poisonous plants, such as hemlock and nightshade; by poisonous fungi and ergot-infected grain; and by the use for food of poisonous fish and molluscs. Each of these poisonings has a pharmacological syndrome peculiar to itself. The commonest form of food poisoning, however, is the gastro-enteritis due to bacterial infection of food or drink, and it is this form which is generally meant in modern usage of the term.

Dyspepsias due to excess or indigestibility of such food as unripe fruit *Dyspepsia* are not included, nor are the infective diseases, such as scarlatina,

diphtheria, enteric fever, tuberculosis, and undulant fever, though all of these may be conveyed by specifically infected food or milk. The illness produced by wholesome foods, such as eggs, milk, or fish, in persons possessing an 'idiosyncrasy' to one or more of these is discussed elsewhere (ALLERGY, Vol. I, p. 334).

Allergic sensitivity

The term 'ptomaine poisoning', formerly applied to illnesses associated with the consumption of food in which bacterial action could be assumed to have taken place, was derived from an erroneous identification of the basic nitrogenous substances, 'ptomaines', produced during putrefaction, with the active toxic principle. It has no literal justification for continued existence in medical terminology.

'Ptomaine' poisoning

2.–AETIOLOGY

Excluding botulism (see BOTULISM, Vol. II, p. 589), which does not present symptoms of gastro-intestinal irritation, two main categories of food poisoning of bacterial origin can be distinguished: (1) those due to infection of the alimentary tract with living salmonellas conveyed by food or drink, and (2) those due to irritative substances, 'toxins', preformed in food or drink by bacterial proliferation. Bacillary dysentery might properly be included in the first category but is a disease distinguishable bacteriologically and, in part, clinically from that produced by the salmonellas; it is discussed, therefore, as a separate entity in this Encyclopaedia (see DYSENTERY, BACILLARY, Vol. IV, p. 317).

3.–BACTERIOLOGY AND PATHOLOGY

(1)—Poisoning from Ingestion of Living Salmonellas

The bacteria capable of producing acute infective gastro-enteritis comprise practically all the salmonellas, with the notable exceptions of the typhoid bacillus and the paratyphoids A, B, and C, which are exclusively human parasites, producing a characteristic continued fever and almost never a violent acute enteritis (see p. 50). The commonest food-poisoning salmonella is that best known in England as the aertrycke bacillus; its usual host is the mouse—hence its original name *Bacterium typhi-murium*—but, if ingested in sufficient numbers, it can produce enteritis and septicaemia, as isolated cases or in epizootics, in almost all mammalian species and in birds. *Bacterium enteritidis*, the Gaertner bacillus, has as its usual host the rat but may occur similarly in most other warm-blooded animals. A score or so of other salmonella types, all capable of producing enteritis in man and other animals, have been distinguished and given specific names, chiefly in virtue of their behaviour in serological tests; among these the Newport, the suipestifer, the Thompson, the morbificans bovis, and the Dublin types are the commonest in England.

Aertrycke bacillus

Gaertner bacillus

Other types

The morphological and cultural characters of the salmonellas are fairly *Morpho-*
uniform and alone almost justify their specific differentiation from other *logical*
bacteria of intestinal origin. They are short Gram-negative rods with *characters*
rounded ends, usually actively motile, and possessing numerous long
lateral flagella; they do not form spores and are readily killed by heat
(a few minutes at 56° C.) and by antiseptics; they can survive for long
periods at freezing point or below but are easily killed by drying and
sunlight. They grow readily on the ordinary nutrient media, their opti- *Cultural*
mum temperature for growth being about blood-heat; they do not *characters*
produce indole, but many types produce hydrogen sulphide in abund-
ance; they ferment dextrose and mannitol (and certain other sugars)
vigorously with the formation of acid and gas but do not attack lactose
or sucrose. Their indifference to lactose as a fermentable sugar is used
in distinguishing their colonies from those of the lactose-fermenting
B. coli; on such solid media as the lactose-neutral-red-bile-salt agar
of MacConkey, inoculated with faeces. the salmonella colony appears
as a pale translucent disc in contrast to the red opaque colony of the
coli-aerogenes group of bacteria. They resist the bacteriostatic effect of
certain dyes, such as brilliant green, in concentrations which effectively
inhibit *B. coli*, and this property is used in their isolation from faeces
and foods. Their natural habitat is the intestine, and their persistence
depends on transference from animal to animal; their pathogenic vigour
under natural conditions appears to vary little.

The immunological behaviour of the salmonellas depends on a highly *Immunology*
complex antigenic system, and the identification of the types corre-
spondingly depends on rather an intricate system of serological testing.

In brief, it may be said that each type has a heat-stable or 'O' antigen- *'O' and 'H'*
complex contained in the bacillary body (hence called 'somatic') and a *antigens*
heat-labile or 'H' antigen-complex contained in the flagella.

The latter complex is divisible into group- and type-specific com- *Flagellar*
ponents; of the group components some six are identifiable, and two *antigen-*
complex
or more of these appear in the majority of the salmonellas, conferring
thus on an agglutinating serum made with any one (with some excep-
tions) the property of agglutinating to some extent all the others. The
type-specific flagellar component, though in some types it is a compound
of more than one antigen, is usually single and, in the main, determines
the type. The phase phenomenon of Andrewes, the spontaneous separa-
tion in a strain of two kinds of bacteria which produce colonies or
culture masses distinguished by the group flagellar complex or the type
flagellar antigen greatly predominating over the other, permits of easy
and reasonably certain identification of 'types' by direct agglutination
tests of type-specific colonies with pure type-specific sera. The 'O' or *Somatic*
somatic complex is of interest scientifically in linking 'types' into some *antigen-*
complex
five large groups which have in common, and predominating in their
O-complex, one or two of some ten heat-stable antigenic components;
practically it is of interest in that the agglutinin response of infected
human beings may be confined to the 'O' antigen; in enteric fever this

is not uncommon and is of importance, as the O-antigen of the typhoid bacillus is almost identical with that of the Gaertner bacillus so common in food poisoning. It will be gathered from this restricted exposition that precise identification of salmonella types can normally be entrusted only to the few bacteriological laboratories specially equipped for the purpose. This identification is of value, however, since it provides the means of tracing the ramifications of an epidemic outburst and of identifying with certainty a salmonella among the other bacteria with somewhat similar morphological and cultural characters which are not uncommon in food products.

Pathogenicity   The salmonellas do not produce a demonstrably potent toxin *in vitro*, and the pathology of the gastro-enteritis which they cause on being ingested is not clear; it probably depends, as in the case of cholera, on an enormous proliferation of the specific bacteria at the level of the intestinal mucosa with consequent inflammatory reaction. Death is produced either by the dehydration and salt starvation consequent on persistent vomiting and diarrhoea or by a septicaemia. Though acute gastro-enteritis is by far the commonest result of ingestion by man of any of the salmonellas in the living state (except the typhoid-para-typhoid group), yet any salmonella type may occasionally produce an illness indistinguishable from paratyphoid fever, with or without a previous acute stage of diarrhoea and vomiting.

Minimal infective dose   As regards the infective dose, data are lacking. In the case of mice it can be shown that a single aertrycke bacillus given *per os* may produce 'mouse typhoid', but it is almost certain, from the irregular incidence of gastro-enteritis among human consumers of the same infected food, that dosage in human food poisoning is an important factor. A similar deduction can be drawn from the fact that a particular sample of infected food, consumed on successive days, may on the first day infect few consumers and produce in these only mild symptoms, but after two or three days' storage—and presumably proliferation of the specific bacteria—the same food may cause severe food poisoning in a high proportion. The necessity of a fairly large dose of the infecting bacteria is in harmony also with the rarity of water-borne salmonella infections, both in man and in domestic animals.

Sources of infection   Salmonellas gain access to human food and drink from three principal sources: (i) animals suffering from acute or chronic salmonellosis may be used insufficiently cooked for food (ducks, pigs, bovines); (ii) animals excreting the salmonellas may contaminate human food with which they come in contact (rats, mice); and (iii) human beings infected from one or other of these animal sources may, with or without concurrent illness, discharge the infective agent for a limited period in their faeces (or rarely in urine) and so contaminate food by handling. Chronic *Carriers*   human carriers are, however, much rarer than in the typhoid-para-typhoid infections.

All these considerations explain the relative frequency with which different articles of food produce the infective type of food poisoning.

Examples of food containing the specific bacteria in considerable *Foods liable* numbers from the first are the meat of cattle or pigs slaughtered while *to contain the specific* suffering from salmonella infection; this appears to be a prominent *organisms* source in Germany but is rather rare in England. Eggs laid by salmonella- *Eggs* infected birds, especially ducks and pigeons, are a common source in all countries and are particularly dangerous, since they may contain very large numbers of the specific bacteria and are often consumed with little or no cooking. Examples of food which, by its nature and the time and temperature of its storage, permits the proliferation of salmonellas casually introduced by rodent or human carriers are pies, hashes, and so-called 'made-dishes' containing moisture and nutritive substances in which bacteria flourish; these, if specifically infected and stored at temperatures over 20 C., may set up typical infective food poisoning. Gelatin solution, much used in the commercial preparation of pies as an addition after baking the pie and hence uncooked, is particularly suitable for the proliferation of salmonellas. But almost any food stored in a warm place for a sufficient time may provide conditions permitting the growth of salmonellas and, if eaten without further cooking, thus become a source of food poisoning. Canned meat products practically never contain living salmonellas and in this respect are among the safest of foods.

(2)—Poisoning from Ingestion of Bacterial Products

The bacteria responsible for this form of gastro-enteritis need not be *Nature of* alive at the time of ingestion: their action depends on the irritative *toxic substance* substances which they have produced in the food or drink during its storage. Nothing certain is known as to the nature of these irritative substances. They are not 'toxins' in the restricted sense applied to the poisons of snake-venom, of certain vegetable seeds (ricin), and of cultures of the diphtheria or the tetanus bacilli, for they can be boiled without much loss of potency. They may be relatively simple chemical substances or, as seems not improbable, they may be actually the autolysed bodies of the bacteria which have lived and died in sufficiently large numbers in the food.

Of such bacteria, producing relatively heat-stable 'toxins', the *Staphylo-* *Staphylo-* *coccus aureus* is the most important species, but its activity as a *coccus* 'toxin' producer is subject to fluctuation. Some races, probably the *aureus* great majority, produce little or none either in ordinary foodstuffs or in the best laboratory nutrient media, whereas others render these substances highly irritating to the gastric and intestinal mucosa; for example, a dose of 10 c.c. of a culture-filtrate may produce violent vomiting on ingestion by man or monkey, though most other species of experimental animal are resistant. It would appear that this gastro-toxic property is not necessarily associated with the presence in large amount in the culture of either the staphylococcal haemolysin or the true toxin (which produces inflammation and necrosis of the skin when injected intradermally and fatal shock when injected intravenously): the

fluctuations in the potency of culture-filtrates in these latter respects do not coincide with the fluctuations in their gastro-toxic content.

Other organisms in this class   Other species of bacteria, including *Staphylococcus albus, Streptococcus viridans, Streptococcus faecalis,* and perhaps the ordinary colon bacilli and proteus species appear also on occasion to be able to render ordinary foodstuffs toxic on ingestion. It is probable that only some, perhaps rare, strains do so in a well-marked degree. But much further experimental work is necessary for a final opinion on the question. All these species are practically ubiquitous; they resist drying and are thus common in dust as well as on the surfaces of man and animals.

It is probable that some of the explosive outbreaks of enteritis in which no bacterial cause can be identified, either in the food or in the patients' excreta, may be occasioned by such growth of normally harmless bac-

Gastro-enteritis due to sewage   terial species. The gastro-enteritis produced, sometimes in very large epidemics, by drinking water heavily contaminated with sewage has probably a similar mechanism, i.e. the production of non-specific poisons by the growth and death of enormous numbers of bacteria in the sewage. A specific causal bacterium has not been demonstrated in outbreaks of this kind.

Foods liable to contain 'toxin'   The foods specially liable to contain toxin produced by the growth of staphylococci and other bacteria are canned meats or fish and potted meat or fish pastes. When these are insufficiently 'processed' so that bacteria survive—and some, at least, of those mentioned have a relatively high thermal death-point—or if the can has a defect permitting their entrance, suitable conditions are provided for growth; the final bacterial content may then be as great as in the best laboratory media. Similar conditions appear to be provided in the pickling of meats, such as salt beef, pressed beef, galantines, and ox-tongues. American experience has shown that foods containing soluble starch, such as sweet cakes, farinaceous custards, and especially 'creams', are particularly liable to staphylococcal infection and 'toxin' production. Milk has also proved a suitable medium for gastro-toxin production by staphylococci. The necessary conditions appear to be: (i) infection of the milk with a toxigenic strain, either from a milker or from a lesion of a cow's teats or udder; (ii) a 'clean' milk which does not rapidly turn sour; and (iii) storage, unpasteurized, for sufficient time at a temperature permitting staphylococcal growth. It may be suggested, though no bacteriological proof has yet been brought, that 'cheese-poisoning' is similarly the result of toxin formation by staphylococci at some stage in the making and ripening of the cheese.

4.–MORBID ANATOMY

There is no characteristic lesion in any of these forms of bacterial food poisoning, apart from general congestion of the intestinal mucosa, especially of the ileum, and the effects of dehydration. The Peyer's patches

are usually swollen but are only rarely ulcerated, even when death is
due to a salmonella septicaemia. The mucosa of the colon may be
almost normal except for a slight excess of mucus.

5.–CLINICAL PICTURE

The symptoms vary very much in severity; it is, in fact, common to find *Symptoms*
in the same outbreak some consumers who entirely escape, others who
are only mildly ill, and still others who suffer to the point of death.

The onset is usually sudden, with abdominal pain, nausea, vomiting, *Onset*
and diarrhoea coming on, after ingestion, in from four to thirty hours
in the case of the salmonella infections and in from one to four hours
in the 'toxin' outbreaks. There are usually associated headaches, cold
sweats, shivering, giddiness, and, occasionally, diplopia: syncope is not
uncommon at the height of the illness, and there is often great prostra-
tion. In the case of the 'toxin' form vomiting and diarrhoea may last for
a few hours only and be followed by very rapid recovery. In salmonella
infections the symptoms usually last for one to four or more days and
recovery is more gradual. In both forms death may result in the acute
stage from syncope or from dehydration and salt starvation, the result
of the continuous vomiting and diarrhoea. In the salmonella infections
death about the tenth day of illness is not uncommon and is due to a
progressive multiplication of the salmonella in the blood-stream and
tissues generally.

In the acute stage the face is pale with drawn features, taking on later *Physical*
in severe cases the 'Hippocratic facies' of extreme prostration. The *signs*
tongue is usually clean at first but soon becomes coated and may later
be raw and dry. The abdomen is universally tender, but there is not any
localized tenderness or rigidity. The vomited material is watery, less
often bile-stained, but in severe cases may show traces of blood. The
stools are watery, usually with faecal staining but occasionally colourless.
Blood is rare in the motions, though it may occur, and the mucus tends
to be rather thin and slimy as contrasted with the tenacious blood-
streaked muco-pus of dysentery. The temperature in the case of 'toxin'
outbreaks is usually normal or subnormal. In the infective type there is,
as a rule, some temporary fever, 99° to 100° F.; in the severe cases this
may be continued for several days or until death. Muscular weakness
may be surprisingly great at the height of the attack and for some time
after, but there are not any paralyses or alterations in reflexes.

Appendicitis is sometimes diagnosed and operated for in cases of *Complications*
salmonella food poisoning. Though specific infection of the appendix *and sequelae*
no doubt occurs in this condition, it is probable that the resulting
inflammation, if any, would always subside without necrosis or other
indication for operation. Salmonella infection may be followed by local
pyogenic conditions, such as empyema, purulent arthritis, osteitis, or
meningitis. Derangement of the alimentary functions with dyspepsia,

constipation, or recurrent diarrhoea may persist for long periods after an attack of food poisoning.

6.–PROGNOSIS

Mortality The mortality varies in different salmonella outbreaks from less than 1 per cent to 10 per cent or even higher; the lower rates, however, are much more common. The very young, the very old, and the invalid are the chief contributors to the death-rate. Although the condition at the height of the symptoms may be most alarming and may practically enforce a guarded prognosis, yet, when improvement has once begun, recovery can be counted upon with some confidence, especially if the temperature returns to normal. As practically all fatal cases show a salmonella septicaemia, a negative blood culture justifies a favourable prognosis. Death is rare in the 'toxin' type of bacterial food poisoning, although the violence of the vomiting and diarrhoea may be even greater than in the infective type.

7.–DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The occurrence of abdominal pain, vomiting, and diarrhoea among the members of a family or other group of persons who have shared a particular meal will usually determine without further question that the illness is some form of food poisoning. The interval between the onset of illness of the first and last of the group rarely exceeds twenty-four hours in salmonella infection and is usually much less, whereas in bacillary dysentery the onset, in successive cases in the group, is often spread over several days. When the onset is almost simultaneous and within four hours of the common meal, the 'toxin' form of bacterial food poisoning is most probably present. Difficulty arises in solitary cases, and in these all the other possible causes of vomiting and diarrhoea may have to be considered. Such solitary cases of infective food poisoning may be due to the ingestion of infected food or drink on some casual and unremembered occasion apart from meals shared with other people. But a common and often unsuspected source is an infected egg, which may form part of a shared meal, though itself not shared. Ducks' eggs in particular have been found infected with salmonellas in such numbers as to produce severe and fatal food poisoning when eaten raw or lightly cooked (fried, whipped, in custard or ice-cream).

Diagnosis from bacillary dysentery It is of some importance, both in treatment and in the prevention of further cases, to distinguish food poisoning from bacillary dysentery (see also DYSENTERY, BACILLARY, Vol. IV, p. 336). In the latter, though the symptoms at onset may be identical with those in the former, vomiting does not last so long and diarrhoea becomes more and more associated with tenesmus. The character of the motions is of help in the differentiation, those of dysentery being usually streaked with blood

(except in the Sonne type, in which this is exceptional) and consisting of rather tenacious mucus in contrast to the thinner slime of the food poisoning case in which, moreover, blood is much less common.

The symptoms of Asiatic cholera (see CHOLERA, Vol. III, p. 179) may *From cholera* in the early stages resemble very closely those of food poisoning: the bowel discharges in cholera are, however, from the first more watery and contain little or no mucus but, instead, the characteristic epithelial flakes.

In all cases of gastro-enteritis due to bacterial infection, laboratory *From other* examination of the faeces or of rectal swabs and of the suspected food, *causes of* when available, will generally settle the diagnosis within twenty-four to *gastro-* *enteritis* forty-eight hours.

Acute poisoning with arsenic or antimony may appear either as *From arsenic* solitary cases or in groups of persons. The symptoms and incubation *and antimony* *poisoning* period may closely resemble those of food poisoning, and the diagnosis may depend on the detection of the act or negligence as the result of which these substances entered the food or drink, or on laboratory tests. In general the symptoms of acute arsenical poisoning resemble those of the infective type of food poisoning; although the former rarely include rise of temperature, vomiting and tenesmus may be even more severe than in food poisoning. Acute antimony poisoning has been relatively common in recent years owing to the use of antimony in cheap enamel water-jugs and pails, the enamel being readily soluble in acid liquids (e.g. lemonades). The symptoms resemble those of the 'toxin' type of food poisoning, the incubation period being very short (thirty minutes), the vomiting very violent, and recovery usually rapid.

Of the other causes of acute gastro-enteritis most will appear as solitary cases. Septicaemias, including pneumonia and general tuberculosis, are liable to display a gastro-enteritis at some stage. An acute peritonitis, especially streptococcal, is often associated with uncontrollable diarrhoea.

Intestinal obstruction due to hernia, intussusception, or volvulus may, *From* especially in children, be attended by the discharge of blood-stained *intestinal* *obstruction* mucus: there will usually, however, be localizing signs in the abdomen which are absent in the gastro-enteritis of food poisoning.

The diarrhoeas due to chill are as a rule mild and rarely so profuse *From* and painful as in food poisoning. Their pathology is obscure, but the *diarrhoea* *due to chill* possibility should not be dismissed that they correspond to the catarrhs of the respiratory tract, similarly associated with chill and exposure, and may be in fact 'virus' infections like the 'common cold'. They are met with especially in mountainous climates, but the so-called 'hill-diarrhoea' of India is most probably a true dysentery due to infection with one of the species of dysentery bacilli (see DIARRHOEA, HILL, Vol. IV, p. 17).

The diarrhoeas of nervous origin and those which appear as terminal *From* symptoms in diabetes mellitus, cerebral haemorrhage, uraemia, cach- *diarrhoeas* *due to other* exia, and severe anaemia, though they may simulate 'solitary' cases of *causes*

food poisoning, should generally be referred without difficulty to the general condition. The help of the bacteriologist will in any case be advisable, and a negative report from him can be taken as decisive when salmonella infection has to be excluded. The same applies to the diarrhoeas due to acidosis, the fermentative dyspepsias, achlorhydria, coeliac disease, ulcerative colitis, mesenteric infarction, and food idiosyncrasies; specimens from cases of all of these conditions are from time to time sent to bacteriological laboratories as possibly from food poisoning.

8.–TREATMENT

A specific therapeutic agent is not yet known either for the salmonella infections or for the toxic effects of the substances produced in food by the growth of staphylococci. Serum-therapy in the former has not yet been sufficiently explored and is not without prospect of success. In the latter all that is known is that, though some degree of active immunity to the gastro-toxin of staphylococci can be induced, humoral immunity has not been observed and an antitoxin which will neutralize the dermotoxic effect of staphylococcus culture does not necessarily affect its action in producing vomiting when given by the mouth.

Treatment, therefore, must aim: (i) at removing the infective or toxic material from the alimentary canal as soon as possible; and (ii) at counteracting the dehydration, salt starvation, and exhaustion which are the immediate causes of death.

Emetics and lavage Emetics are rarely indicated, but free lavage of the stomach with a warm solution of sodium bicarbonate (1 drachm to a pint) is a useful sedative, especially in young children with continued vomiting. Castor oil in doses sufficient to ensure purgation ($\frac{1}{2}$ to 1 fluid ounce) should be given without delay in every case in which the diagnosis of food poisoning is reasonably certain and the exhaustion of the patient not too far advanced. When vomiting prevents its successful administration, calomel or mercury with chalk in purgative doses may be given instead. Morphine hypodermically or tincture of opium by the mouth should be given to relieve the pain. Persistent diarrhoea should be treated with teaspoonful doses of bismuth carbonate or bismuth subnitrate or with aromatic powder of chalk. Powdered charcoal also may be found useful in checking diarrhoea.

Administration of saline Dehydration and salt starvation require the infusion intravenously or subcutaneously of sterile saline solution, preferably containing 5 per cent dextrose. Bouillon or egg albumen solution strongly salted may be *Stimulants* given at the same time by mouth. Stimulants such as wine (champagne or burgundy), brandy, or whisky may be required to combat the intense exhaustion following the acute stage and should be given in frequent small doses. Injection of camphor (10 to 30 minims) subcutaneously may be necessary for syncope.

Diet During convalescence progress from a purely liquid diet to normal

food should be made very carefully, especially in cases in which the gastro-enteritis tends to relapse or is slow to subside. Cases in which the temperature continues above normal should be treated in the same manner as cases of enteric fever.

Patients with food poisoning due to salmonella infection should be nursed with the same precautions in the disposal of excreta as patients with enteric fever, and persons liable to come in contact with such excreta should preferably not be allowed to prepare or handle food for others, however carefully hand disinfection may be practised. The period of infectivity of faeces from cases of salmonella infection is, however, much shorter than in the enteric group, and precautions can usually be relaxed without risk when clinical recovery is complete. *Disposal of excreta*

The practitioner called in to attend a case of food poisoning should regard it as his duty to notify the local Health Officer and to arrange, if possible, for specimens of suspected food and of the patient's excreta to be put aside for bacteriological examination. *Notification of Health Officer*

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FOOT AND MOUTH DISEASE

See APHTHOUS FEVER, Vol. I, p. 709

FOOT, DISEASES AND DEFORMITIES

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Reference may also be made to the following titles:

ARTHRITIS

ATHLETICS AND ATHLETIC
　INJURIES

BIRTH PALSIES

BONE DISEASES

CORNS AND BUNIONS

DISLOCATIONS AND
　FRACTURES

EPIPHYSES, DISEASES
　AND INJURIES

FOETUS DISEASES

FROST-BITE AND
　TRENCH-FOOT

FUNGOUS DISEASES

HAND, DISEASES AND
　DEFORMITIES

JOINTS, DISEASES AND
　DISORDERS

MYCETOMA

NAILS DISEASES

TALIPES

1.–DEFORMITIES

520.] The major deformities of the foot, congenital and acquired, which fall under the heading of talipes, are dealt with in the appropriate section (see TALIPES).

(1)—Aetiology

The foot, being a part of the body which is undergoing fairly rapid evolutionary change, is subject to considerable variations in its normal anatomy. Any study of deformities of the foot would be incomplete unless it made some mention of these, because many disabling conditions either arise from them or are secondarily dependent upon them, as far as their distribution and severity are concerned. *Evolutionary variations*

In about 70 per cent of feet the great toe is the longest, i.e. projects further forwards than the others, but this is of less practical importance than the fact that in about 52 per cent the head of the second metatarsal projects beyond the others, and the first projects further forwards in 30 per cent. The line of the metatarsal heads forms the hinge about which the foot moves on the toes as the foot rises to the 'take-off' position during walking, and it is there that most of the forces are applied to the ground. The position in which callosities develop will thus depend upon this variation in the relative prominence of the metatarsal heads; the development of hammer-toe is also, although less directly, determined by the same factor. *Relative prominence of metatarsal heads*

Variations also occur in the ossification of the bones and in the presence of supernumerary bones, which are stated to occur in 25 per cent of human feet. Their practical significance is that they may be mistaken radiologically for fractures or pathological conditions. Fusion of bones *Ossification*

is seen especially in the phalanges of the fourth and fifth toes and is often associated with a congenital contracture of these toes, which are undergoing a relatively rapid evolutionary shrinkage.

Gross deformities of the foot are seen in congenital absence of the tibia or fibula and are due to lack of adequate support at the ankle (see Vol. II, p. 559).

In some extrapedal conditions, e.g. achondroplasia (see Vol. I, p. 139), acromegaly (see Vol. I, p. 167), the feet are affected, and in association with spina bifida (see SPINAL CORD DISEASES) the most severe talipes may arise. In patients who survive, trouble appears later in life from the development of callosities, pathological dislocations of the toes, and disturbances of vasomotor and trophic control.

(2)—Congenital Deformities
(a) Supernumerary Digits
521.] The commonest of these is the presence of supernumerary digits, which are usually found on the outer, occasionally on the inner, border of the foot. They are of various sizes, from a small pedunculated nodule to a completely developed extra toe. One extra digit is the rule, but as many as thirteen digits have been recorded. As they tend to run in families, the defect cannot be due to any local disturbance during foetal life.

(b) Suppression of Digits
Lobster-claw   Suppression of toes, usually the fifth, is sometimes seen, and in the condition usually called lobster-claw deformity the second, third, and fourth toes are suppressed, but the fifth is hypertrophied and equals the first, to which it is opposed.

(c) Syndactyly
Syndactyly occurs less often than in the hand and is obviously of much less importance. The fusion may consist merely of an increase in the normal web, or it may involve all structures, including the bones. It is often associated with webbed fingers and is decidedly familial in its incidence. (See Vol. II, p. 560, and HAND, DISEASES AND DE-FORMITIES.)

(d) Hypertrophy
Hypertrophy (macrodactyly) may involve one or more toes. The increase is usually due to the overgrowth of soft parts, the bone being only slightly enlarged.

(e) Cleft Foot
Cleft foot occurs when the incorporation of the first toe into the rest of the foot, which is the most recent event in the evolution of the human foot from the prehensile foot of an ape-like ancestor, fails to occur. Its relation to the lobster-claw deformity is obvious.

(f) Treatment

Most of these deformities do not require treatment: in others the treatment is purely symptomatic.

Supernumerary digits, when small, should be removed in infancy: when the additional toe is well developed and functioning it may remain, but if it is unilateral the question of its removal must be considered on economic grounds, for the greater size of one foot makes it impossible for the patient to wear ready-made shoes. An hypertrophied toe may be reduced in size by operation, or it may be amputated. *Supernumerary digits*

Webbing causes very little disability in the foot and rarely requires treatment; if it should be thought necessary, the operations are conducted in the same manner as those for the fingers (see HAND, DISEASES AND DEFORMITIES). *Syndactyly*

(3)—Acquired Deformities

(a) *Flat-Foot*

522.] It is surprising that in an account of a condition so well known *Definition* and long studied as flat-foot it immediately becomes necessary to discuss not only its aetiology but also its essential nature. There is no precise definition of flat-foot; whereas some would include eversion and abduction of the anterior half of the foot, resulting, for instance, from paralytic diseases, others would very definitely exclude this form. As usually accepted the term refers to an acquired deformity in which, in the absence of gross organic disease, the inner border of the foot drops and the arch, which is normally present there, becomes flattened in various degrees. This arch varies enormously in its development from one person to another without being in any respect pathological or disabling, and many cases at present treated as flat-foot are really due to other painful conditions occurring in a foot which has always had a very low arch.

In a well-marked case the chief points in the morbid anatomy are a *Morbid anatomy* downward subluxation of the head of the talus (astragalus) between the calcaneus (os calcis) posteriorly and the navicular anteriorly. This is necessarily accompanied by an elongation of all the structures passing along the inner border of the foot, particularly the plantar (inferior) calcaneonavicular ligament, sometimes called the spring ligament. This elongation produces an abduction of the anterior half of the foot, which is also everted. At first the displacement is present only during weight-bearing, but subsequently it becomes a constant deformity with the development of secondary bony and articular changes.

The older hypotheses regarded this as a static deformity due to loss *Aetiology* of strength in the ligaments, tendons, and fasciae which, it was presumed, supported the arch, a condition arising as a result of abnormal strains thrown upon this region especially during the period of growth or in debilitating diseases. The modern view, which has very largely

supplanted the older ideas, regards the arch of the foot as a dynamic or postural structure dependent for its maintenance upon muscular activity and tonus. According to this view the arch in a perfectly natural foot should appear and disappear as the muscles, particularly the tibialis posterior, contract and relax. In support of this view is Keith's work upon the evolutionary changes undergone by the foot as it became converted from the prehensile organ of our ape-like ancestors to the supporting human foot as we know it. He showed that the arch, an essentially human structure, might have been pulled up (racially) by a diversion of the action of certain muscles previously used for prehensile purposes, and he assumed that these same muscles were responsible for the maintenance of the arch.

The fact that the arch does not actually appear and disappear with facility in the ordinary foot is explained in this view by the development of a secondary rigidity produced by the restricting effects of foot-gear.

I cannot accept the newer ideas, and consider that the relative rigidity of the human foot is but an indication of an evolutionary tendency which is destined to produce an even less flexible structure for the mere purposes of locomotion in the future. The development of the essentially human arch to the foot I believe to be the result not of a muscular uplifting but of the downward and backward growth of the equally human heel necessitated by the adoption of the upright posture.

At present there is not any justification for dogmatism concerning these conflicting views; the arguments in favour of each are fully laid out in the books mentioned in the list of references (see p. 437). Unfortunately this divergence of opinion is of more than theoretical interest, because the treatment of flat-foot should directly depend on its pathology, whereas at present it is possible to conduct treatment upon an empirical basis only.

Diagnosis   The diagnosis of flat-foot is derived not only from observation of the condition of the foot at the time of examination but also from knowledge of the changes which the history of the case shows to have occurred recently. The well-marked case is very obvious, but in the early stages it may need a good deal of discrimination to decide if pain and slight disability in the foot are really due to flattening. The practitioner should regard the diagnosis with suspicion until all other possible causes of the symptoms—e.g. Köhler's disease (see p. 436)—have been excluded by careful clinical and radiographic examination. In estimating the severity of the condition it is necessary to note the variation in the arch with activity, when bearing weight and when at rest, and then to test what degree of reduction is possible upon manipulation. For following progress an imprint of the sole is useful and may be prepared in any convenient way (see Fig. 92).

In a true case of flat-foot attention must also be paid to the patient's general state of health, his occupation, and what it entails in the way of foot strain; a history of recent illness or of increase in weight is important. All cases should be examined radiographically, not only

to exclude certain congenital anatomical abnormalities of the bones
but also to estimate the degree of bony and arthritic changes which
are almost invariably present in long-standing cases.

Many attempts have been made to classify flat-foot. but none of them *Classification*
is entirely satisfactory. It is, however, very essential to distinguish
certain types of case and also to have some record of the severity of
the condition. The following classification, although not exhaustive.
may be found useful: (i) congenital. really atavism reproducing the
stage reached by the orthograde apes: (ii) infantile, said to be due to
delay in the development of sufficient muscular power to pull up the
arch: actually flat-foot of the infant is more apparent than real, the
arch being obscured by fatty pads: some of the cases are examples of

<p align="center">(a)   (b)   (c)   (d)   (e)</p>
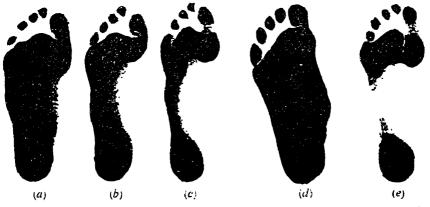
FIG. 92.—Imprints of the sole; *a*, *b*, and *c* from normal feet with low, medium, and
    high arches respectively; *d*, from case of flat-foot, showing abduction of fore part
    of foot: *e*, from case of pes cavus. (The illustrations to this article are from the
    Author's *The Foot*)

lowly arched normal feet; the type associated with a short tendo
Achillis is a sub-group; (iii) adolescent: two types occur at this period,
both being associated with rapid increase in weight and stature and
the beginning of occupations entailing prolonged standing or other
bearing of extra weight; in one type the arch drops in the way already
described; in the other there is an intense spasm of the peroneal muscles
(spastic flat-foot) (see p. 419); (iv) infective, including cases following
influenza, tonsillitis, and enteric; focal infection also is thought to bear
an aetiological relationship, and gonorrhoea by its local effect upon the
soft tissues of the joints is a well-recognized cause of acute flat-foot
(see p. 419): and (v) adult, in which the condition has often been
present for some period before the onset of pain and tenderness attract
attention. It is particularly likely to be associated with gross arthritic
changes (rigid flat-foot) and occurs in middle age when weight tends to
increase and there is lack of exercise.

The recognition of three stages is useful in determining treatment: *Three stages*
(i) the foot appears normal when at rest, but the arch becomes unduly
depressed upon weight-bearing; (ii) the arch is depressed with the foot

at rest, but it can be returned by simple manipulation with the hands; and (iii) the arch is permanently depressed, and nothing short of powerful mechanical wrenching has any apparent effect upon it; there are, however, often extensive bony changes which make wrenching inadvisable.

Treatment   Owing to the great diversity of opinion regarding the origin of the condition it is impossible to be dogmatic concerning treatment. Many methods of treatment at present used are undoubtedly founded upon false ideas of pathology. There is, however, a general agreement that exercises, massage, electrical stimulation, and manipulation are of value *Exercises* in the earlier stages. Simple exercises, such as rolling on to the outer borders of the feet and back and rising on the toes, should all be conducted with the feet pointing slightly inwards. Re-education of the patient's attitude when walking and standing, all tendency to turn the toes outwards being corrected, is important. All periods of prolonged standing should be avoided, and occupations involving them must be abandoned. In more severe and acute cases a preliminary period of complete rest is essential; sometimes a temporary plaster splint is *Mechanical* advisable. The use of mechanical supports to the arch has occasioned *supports* great controversy. By many they are strongly condemned and stated to lead to further weakness of the supporting muscles and undesired rigidity. Nevertheless, there cannot be any doubt that very many patients find the use of such supports beneficial; therefore, before they are indiscriminately condemned, the reason for their giving such apparent comfort should be examined. Some supports are quite rigid, others are resilient; if it is decided to use them, the former type will be found more useful in the severe cases with rigidity, and the latter may be used in the earlier cases. A good support should be constructed for each patient from a cast of the foot in the corrected position. Specially constructed boots having the inner border of the heel raised and carried well forwards beneath the instep, the upper being strengthened under the arch, are often used. According to the newer hypotheses, all types of support are wrong in that they tend to limit the 'natural' mobility of the foot. Since holders of these views believe that the pain and disability are caused by the inability of the arch to descend, they quite logically advocate forcible breaking down of the arch to restore complete mobility in both directions, followed by the necessary exercises to maintain this new mobility. Whatever view is taken, it will be found *Manipulation* that manipulation of the foot under anaesthesia is often a valuable preliminary method of treatment in more advanced cases which do not respond to simpler forms of treatment. For the most advanced cases, in which the deformity is complete, it is often best to do nothing. *Surgery* Operative measures, i.e. cuneiform tarsectomy, have been used in these cases, but, except for the cosmetic result, they are of doutful value. A *Plastic* recently devised treatment is by means of a plastic support made of a *support* rubber-like vegetable mass which, after previous warming, is applied to the sole. The patient then walks upon it while it becomes solid. In

this way the soft structures and muscles form individual grooves in the support, so that their normal functions are not disturbed. It is as yet too early to say whether this idea is theoretically and practically sound.

Despite the indefinite nature of the advice regarding treatment, which of necessity arises when conflicting opinions of pathology are held, the practitioner will find that more failures arise from mistakes in diagnosis than from deficiencies in treatment of the true cases. Often the treatment will involve the trial of several methods either seriatim or simultaneously.

Spastic flat-foot

Although this condition has been included above as one of the types *Aetiology* of adolescent flat-foot, it is really an entity with an obscure aetiology. It is seen in overgrown adolescents of poor general physique. The foot is drawn into a position of eversion by spasm of the peroneal muscles, and great pain and tenderness are present on both sides of the instep. It is usually agreed that the spasm is caused reflexly from an inflammation in the transverse tarsal (mid-tarsal) joint: the injection of a local anaesthetic into this joint often temporarily abolishes the spasm and may be used as a diagnostic test. In some cases there is a congenital fusion of the calcaneus and navicular which leads to a synovitis of the talo-calcaneonavicular joint; this condition and other congenital abnormalities possibly bearing an aetiological relationship must be searched for radiographically. A toxic synovitis from focal sepsis in the tonsil or elsewhere is another possible cause. Probably most cases arise from a combination of a structural abnormality, e.g. extreme obliquity of the line of the metatarsal heads, with the same aetiological factors which in a normal foot produce adolescent flattening.

Treatment proves to be very tedious. If the occupation involves long *Treatment* standing, nothing short of a complete change is likely to be of any avail. Manipulation, heat, massage, and particularly rest (possibly by plaster splinting) are all useful in the earlier stages. Septic foci must be removed. In severe cases a complete cure is rarely obtained, and reduction of the deformity may be impossible until the peroneal tendons have been divided. Crushing of the motor nerves or their injection with alcohol is sometimes used in advanced cases to paralyse these muscles. In any event the use of wedged boots with outside iron and T-straps is advisable for a prolonged period after the deformity has been reduced.

Acute flat-foot

In these cases the dropping of the arch occurs with great rapidity *Association* and may be practically complete in a few days. The most marked *with* example is seen in gonorrhoea, when it may occur either at the end *gonorrhoea* of the acute stage or subsequently, especially following instrumentation. After prolonged illnesses the arch may drop rapidly when the patient gets on his feet again; therefore preliminary exercises and the temporary use of soft supports are advisable.

Another form of extremely acute flat-foot comes on suddenly in those undertaking some unusually strenuous march or walk; a lancinating pain develops under the head of the talus (astragalus), but there is little to be seen on examination. Support to the arch, however, affords almost instant relief, thus proving the nature of the condition.

(b) Hallux Valgus

Definition
Aetiology

The outward deviation of the great toe, to which this term is applied, is one of the commonest acquired deformities of the foot. Its aetiology is still uncertain. The simple hypothesis, accepted until recently, that the deformity was due to the pressure of foot-gear does not explain many of the features associated with the condition, or its incidence and distribution. The most probable hypothesis is that the deformity of the toe is one manifestation only of the graver deformity affecting the whole anterior half of the foot, namely, a splay of this region and especially of the first metatarsal from the others. This hypothesis assumes an evolutionary factor, for the incorporation of the first metatarsal into the rest of the foot is the most recent evolutionary change in the development of the human foot from the more highly specialized prehensile foot of an ape-like ancestor with its separate great toe. According to this hypothesis, therefore, splay-foot is an atavistic condition which becomes evident if the anterior half of the foot is subjected to strains beyond its capacity, such as may arise from the wearing of high heels. When the first metatarsal splays, the phalanges would be carried with it but for the restraining influence of the intrinsic musculature, chiefly the adductors, and, of course, of the foot-gear. A deviation of the great toe must result and is usually associated with a rotation, also fundamentally atavistic, with the result that the nail looks inwards instead of upwards. The hypothesis thus combines an intrinsic evolutionary weakness, which will vary in degree from one person to another, with a local factor depending upon the use of foot-gear. A little thought devoted to the problem shows that this hypothesis is capable of explaining the incidence of the condition and all its associated features.

Splay-foot

Incidence

As would be expected from these considerations, the condition is much commoner in women than in men, but if the evolutionary stability of a foot is poor the deformity may develop without the additional strain produced by wearing high heels; thus it may be found in women who have never abused their feet, in men, and even among primitive and other habitually unshod peoples.

The chain of events leading to the deformity probably starts in the late adolescent period, but the initial stages are painless, and the patients do not usually present themselves for examination until middle life, when the onset of complications produces disability.

Morbid
anatomy

The morbid anatomy consists of an outward subluxation of the proximal phalanx upon the head of the metatarsal with shortening and lengthening of the outer and inner ligaments respectively (see Fig. 93).

On the inner aspect of the head of the bone a bone-forming periostitis produces an exostosis, over which an adventitious bursa forms in the subcutaneous tissues. The long tendons are displaced outwards, and in the case of the flexor muscle this is associated with a corresponding displacement of the sesamoids, so that the outer bone frequently lies in the interosseous space. Sooner or later the joint displays well-marked osteoarthritic changes.

In many cases the second toe is contracted to a 'hammer' deformity, a change directly connected with the increased weight-bearing which the second toe now has to undertake (see p. 423). Under this toe, and
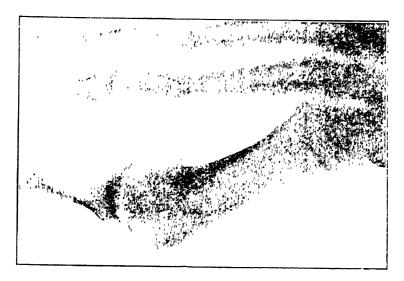
FIG. 93.—Radiograph of hallux valgus. Note increased width of first interspace, and displacement of outer sesamoid into interosseous space

often under the third also, callosities develop which in themselves are a sufficient indication of the change in the weight-bearing areas.

Patients seek treatment for this condition either on account of pain *Treatment* and disability or for aesthetic reasons. It cannot be too strongly emphasized that the primary deformity is a splaying of the anterior metatarsal region and that the treatment of this must first receive attention; treatment of the valgus deformity alone cannot be entirely satisfactory unless this is borne in mind. The mere reduction of the *Reduction of* splay, even temporarily, immediately tends to correct the deviation of *splay* the toe although, owing to secondary changes in the joint, this cannot be more than partial. With this proviso, treatment of the deformity may now be considered. The multiplicity of the methods advocated is a sure indication of the intractable nature of the complaint. In minor *Local* cases the use of correcting springs, straps, and pads may be all that is *treatment* required; the application of a correcting sandal at night is valuable, especially in children, and the old-fashioned toe-post in the shoe still has its advocates. A skilful chiropodist can often help by appropriate

padding in these cases, and also in the very severe cases in which operation has not succeeded in giving relief.

Operation   Operative treatment may be undertaken for the correction of the deformity or for the relief of complications. The chief complication is a bursitis (bunion), the treatment of which has already been dealt with (see Vol. III, p. 435).

While entering into details of surgical procedures it may be stated that it is a mistake to adopt any one stereotyped operation for this condition. Pain and disability are due to many different causes, e.g. arthritis, sesamoid displacement, and bursitis; the operation should be designed to deal with the particular cause. The operation usually performed consists in removal either of a portion of the head of the metatarsal or of the base of the phalanx; probably the latter gives slightly better results. In some cases, however, removal of the sesamoids, either alone or combined with other procedures, is advisable; in others a simple reduction of the exostosis will give the desired result. Most of the operations produce their effect by reducing the deforming pull of the intrinsic muscles upon the toe either by shortening the digit or by performing what is virtually a tenotomy of these muscles.

Results of   In the assessment of results it must not be overlooked that in a con-
operation   siderable proportion of these cases in which the head of the metatarsal is excised the patient never again uses this joint for the 'take off'. This effect is obscured by the fact that she cleverly learns to transfer the weight to the outer border of the foot and even to walk comparatively well in this way. If the gait is closely observed, however, and the position of the callosities on the sole of the foot is carefully noted, it will be conceded that, in as much as the patient cannot now walk on the first metatarsal joint, the operation is really a failure.

Finally it must be reiterated that none of these operations is complete or satisfactory unless combined with proper treatment of the causative splay-foot. It is not to be expected that a splay which has taken years to develop will be remedied easily; indeed in many cases permanent cure cannot be looked for. Support should be given to the metatarsal region by the use of circumferential strapping or webbing, and in every instance this should be combined with a well-cut metatarsal pad of felt lying under the necks of the central three bones. Shoes should be particularly snug round the instep and may also be fitted with a metatarsal pad built into the inner sole. Exercises and electrical stimulation of the muscles of the sole also help.

(c) *Hallux Rigidus and Hallux Flexus*

Definition   The metatarsophalangeal joint of the great toe quite often becomes rigid in cases of hallux valgus, owing to the secondary arthritis, but here the limitation of movement is overshadowed by the main deformity, and the above terms are usually restricted to cases in which there is little lateral deviation of the toe.

Aetiology   The underlying pathological lesion is an osteoarthritis of the joint with

the formation of pronounced bony ridges, which are most marked on the dorsal aspect. As in hallux valgus, this is a wear-and-tear arthritis, due to the excessive strains falling on this joint in certain predisposing conditions, such as elongation of the inner border of the foot when the arch drops and abnormal length of the first metatarsal. Fixation of the joint in the flexed position is obviously more disabling than fixation in extension, so most cases seeking treatment display a rigid flexed toe. The gait is extremely awkward, the foot being rolled over on to its outer border in walking, so producing a callosity under the fifth metatarsal head.

The diagnosis is obvious, but a careful study of radiographs is *Treatment* necessary before deciding upon the best method of treatment. In early cases a good deal can be done by the use of pads and a metatarsal bar to protect the joint from further strain; if radiography reveals little bony change, manipulation under anaesthesia is advisable; but in severe cases operative treatment should be used. Although the pro- *Operation* cedure is almost identical with the standard operation for hallux valgus, the results on the whole are more satisfactory, as there is no underlying splay to be dealt with.

In childhood and adolescence a spastic rigidity of the toe may occur *Infantile* in which there are no radiological changes to be noted. These cases are *form* usually associated with synovitis of the joint, sometimes due to injury, e.g. stubbing the toe, or to a blood-borne infection from septic tonsils, teeth, or other foci. The treatment consists of rest for a short period, local heat, and the removal of septic foci.

(d) Hammer-Toe

In hammer-toe there is hyperextension at the metatarsophalangeal joint *Definition* and flexion at the proximal and extension at the distal interphalangeal joint. Sometimes the distal joint remains straight, and the tip of the toe impinges upon the ground with the development of a subungual corn (mallet toe). A corn with an underlying bursa invariably develops over the prominent proximal joint. Secondary shortening occurs in the skin of the plantar aspect, the volar (glenoid) ligaments, and the flexor tendons. The condition may involve one or several toes. In the former case the second toe is most commonly affected, particularly in association with hallux valgus, but there is sometimes a definite familial tendency, and in claw-foot all the toes display the hammer deformity.

The mechanism of production of the ordinary hammer-toe is debatable, *Aetiology* but it seems probable that it depends upon an exaggeration of a movement normally present. As the foot rises to the 'take-off' position, the tips of the outer four toes are held firmly on the ground, and the heads of the metatarsals roll forward and force the toe into the flexed position. Owing to the presence of the sesamoid bones, this rolling does not occur at the first metatarsal head, where the movement is one of pure rotation about a fixed axis. If, following the development of a hallux valgus, the second metatarsal is called upon to carry the body-weight,

the forced flexion of the toe is exaggerated and hence established permanently.

Treatment   The management of hammer-toe depends upon the associated conditions. In claw-foot attention must be paid to the general architecture of the foot to which the deformity of the toe is secondary (see TALIPES). When a single toe is involved, and in the early stages, a skilled chiropodist can do much to depress the proximal bone and to elevate the others by the use of felt pads. A night sandal, in which the deformity is held corrected by straps, is also useful in this stage.

Operation   For the fully developed condition operative treatment is usually necessary. The accepted orthopaedic formula, that a hammer-toe should never be amputated, need not be obeyed too rigidly if all the circumstances of the case have been given due consideration. For cases associated with hallux valgus, however, a conservative operation for straightening the toe is best. Excision of the proximal interphalangeal joint and the 'spike' operation of Higgs both give good results in suitable cases and are combined with removal of the callosity and bursa (see Fig. 94). The rare cases in which multiple hammer-toes are secondary to paralysis of the intrinsic muscles are dealt with by padding and straps to relieve local pressure. Operations for cases associated with pes cavus are discussed under the title TALIPES.

FIG. 94.—To illustrate Higgs's spike operation for hammer-toe

(e) Ingrowing Toe-Nail

Definition   In minor degree this condition, also called onychocryptosis, is extremely common. It consists of the folding over of the soft structures of the lateral nail-groove and is commonly ascribed to wearing tight *Aetiology*   pointed shoes or hose. As, however, many cases occur in which the foot-gear does not show any of these characters, it is clear that there must be other factors of importance.
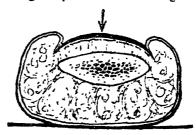
The nail-bed is very intimately attached to the terminal phalanx, and when this bone is pressed on the ground in walking the nail of necessity tends to be embedded in its surroundings (see Fig. 95). In this way the primary roll-over of the soft tissues round the nail-edge occurs, and the condition will be accentuated in the presence of tight foot-gear. If the nail is not cut the distal portion will lie over the terminal pulp, and so the tendency to embedding will be resisted, an observation that has been applied to the treatment of the condition. For obvious reasons the great toe will be the one usually affected. The ingrowing nail alone produces little discomfort, but the presence of complications renders

the condition troublesome. To a large extent these depend upon the difficulty of cutting the embedded nail right up to its lateral edge, so that a small pointed projection (the so-called splinter) grows forwards into the soft tissues, penetrates the skin, and introduces infection (see Fig. 96). The inflammatory oedema which follows buries the nail still deeper. Apart from infection, a troublesome corn may arise in the groove from the rubbing of the rolled-over skin against the nail.

Several homely measures, more or less efficacious, are used in this condition: cutting the nail straight across instead of in a curved fashion, thinning the centre of the nail by scraping, cutting a deep V down the centre of the nail; but none of these is of more than popular interest. Some cases are best left alone, the patient being instructed how to cut the nail to avoid splinters, and foot-gear of adequate size being adopted. A piece of lint or thin malleable metal

Treatment

FIG. 95.—Transverse sections through terminal phalanx of great toe. In the upper drawing the effect of the downward pressure in producing ingrowing toe-nail is shown. Note especially the intimate attachments of the nail-bed to the bone, and the arrangement of the fibro-fatty loculi under the terminal phalanges of the toes

passed under the nail-edge and brought out over the skin fold is of value.

Usually infection is present before the patient seeks advice; a search must then be made for the presence of a splinter, which should be
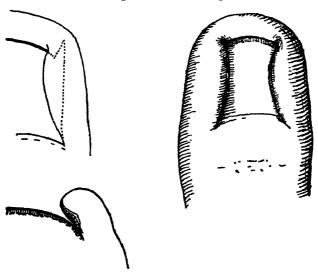
FIG. 96.—Diagrams illustrating production of 'splinter' at lateral margin of ingrowing nail; lower left-hand diagram shows formation of corn in lateral nail-groove

Operation

removed with fine forceps, aided by scissors or a thin chisel. The infection is treated by the usual antiphlogistic measures. At a later date operative treatment with a view to a radical cure may be undertaken. When the nail can be preserved, the excision of a complete wedge of

tissue, including the edge of the nail and the fold of skin, and extending back to the nail-root, gives good results (see Fig. 97). In persistent and advanced cases removal of the nail-bed is advocated, but there can be no doubt that for these the best treatment is amputation through the terminal phalanx, using
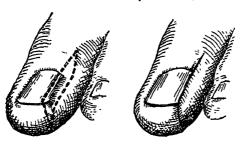
FIG. 97.—To illustrate the wedge operation for ingrowing toe-nail

a long plantar flap. This leaves the patient with a nailless toe, shortened by but half an inch, and has no effect upon the gait; it is, moreover, a certain cure.

(f) Ram's-Horn Nail

Aetiology

This condition, also called onychogryphosis, is practically limited to the nails of the toes, particularly the great toe, and often follows injury; a solitary trauma will suffice, e.g. the tread of a horse's hoof (hence the term ostler's toe), but commonly there is a minor intermittent impact, produced by a short boot or by crowding of the toes. In a few cases a history of injury or infection cannot be obtained. It is also occasionally seen in aged bedridden patients, particularly women, and variously ascribed to lack of attention, weight of bedclothes, and other causes, but it is probably due to vascular changes in the nail-bed. In all
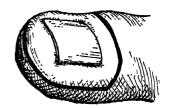
FIG. 98.—To illustrate incision for amputation of terminal phalanx

cases the condition is probably due to hyperaemia of the proximal and ischaemia of the distal portions of the nail-bed.

The horn may continue to grow until a circle is almost completed, but usually treatment is adopted before this extreme is reached. The nail may be accidentally wrenched off; more frequently this is a result of surgical activity; in either case the condition is reproduced. Ulceration may occur about the base and sometimes ends as a malignant subungual growth.

Treatment

In elderly and bedridden patients palliative treatment is proper; the nail may be reduced by an electric drill and burr, a fine saw or, more tediously, by a suitable pair of nippers. In less severe cases a preliminary softening with solution of potassium hydroxide (B.P.) for an hour or so may enable the removal to be performed by scissors and scalpel. In younger patients the quickest relief is obtained by removal of the whole

nail, followed by excision of the nail-bed; but, owing to the difficulties of dissecting out the irregular nail-bed, spicules of nail frequently remain, and there is no doubt that the most satisfactory treatment is amputation through the terminal phalanx, using a long plantar flap (see Fig. 98).

(g) Subungual Exostosis

This consists in the outgrowth of a small bony tumour under the nail- *Definition* bed at the tip of the toes, especially the great toe. The cause is not certainly known; it has been variously attributed to trauma, chronic *Aetiology* infection, arthritic changes, or dichotomy of the terminal phalanx. The growth first appears under the distal half of the nail and then forces its way between the tip of the nail and the terminal pulp, being covered by a layer of hard desiccated tissue, which may later separate and expose the bone to view. X-rays show an outgrowth of cancellous bone with but little demarcation from the phalanx.

Treatment is called for on account of pain and disability. Small out- *Treatment* growths can be removed through an incision skirting the nail-edge, but in more advanced cases it is best to amputate the distal two-thirds of the terminal phalanx, using a long plantar flap, for the nail-bed in these cases is distorted and, if retained, may produce a thick troublesome nail, whereas the loss of the end of the phalanx does not produce any disability.

2.–INJURIES

523.] Injuries of the foot, despite the fact that in human beings it is no longer a prehensile organ, are commoner than might be expected. This is undoubtedly because the various protective mechanisms, which withdraw the hand so readily from potential danger, are less developed in the foot, and in addition the foot is usually carrying the body-weight and so cannot be withdrawn rapidly enough to avoid injury.

Injuries to the bones and joints are dealt with elsewhere (see DISLOCA-TIONS AND FRACTURES and JOINTS, INJURIES AND INTERNAL DERANGE-MENTS). In the case of the soft parts, incised wounds are usually found *Incised* on the dorsum, and, as the foot-gear has been penetrated, it is common *wounds* to find foreign bodies, such as leather, embedded in the wound. Occasionally one of the large dorsal veins is divided, and bleeding is profuse. The other structures are here very superficial, and tendons, nerves, and arteries are thus often implicated. Such damage must be carefully ascertained and, if the general condition of the wound permits, dealt with by immediate suture. Should there be any doubt as to the cleanliness of the wound, it is better to delay suture and to treat by packing with antiseptic (flavine) gauze until the risk of infection has passed. The ends of divided tendons and nerves may have a stay suture passed through them to prevent retraction and to aid identification at the secondary operation. Cleanly incised wounds of the sole are rarer; if the resulting scars are situated over areas subject to pressure they may

become tender and cause considerable disability. For this same reason any incision made by the surgeon should avoid these areas.

Crushing wounds Gross damage to the soft parts is often the sequel of a motor accident; jagged gaping wounds may be found on any part of the foot. There is usually considerable damage to tendons and muscles, the former being sometimes completely avulsed from their muscle bellies in the leg. These wounds must be immediately treated by the removal of all dead and severely damaged tissue and then packed lightly with flavine gauze. It is wrong to attempt immediate suture and to omit prophylactic injection of tetanus and gas-gangrene antitoxin. The skin and subcutaneous tissues are sometimes lifted as a flap by the passage of a rubber-tyred wheel over the foot; if the pedicle of attachment is distal the skin usually undergoes necrosis, but with a proximal pedicle there is a hope that a portion of the flap will survive. Subsequent skin-grafting will almost certainly be necessary, and if a weight-bearing area is concerned, e.g. the heel, nothing short of a whole thickness pedicle graft, raised from the opposite thigh and transferred in stages, will withstand the body-weight without trouble. Elsewhere Thiersch grafts are adequate. Direct traumatic gangrene may follow crushing injuries when the blood-supply to the part has been interfered with, but spreading gangrene may also follow infection with gas-gangrene organisms.

March foot The special fracture of the second or third metatarsal, known as march foot or *pied forcé* and due to repeated small injuries, is described elsewhere (see Vol. IV, p. 171); the only other fracture needing attention *Fracture of* here is that of the sesamoids of the great toe. This injury is produced by *sesamoids* jumping onto the toes, and its chief interest lies in the mistakes which may arise in radiological diagnosis. These bones often have more than one ossific centre, and the appearance in the film closely resembles a fracture. The condition is not always bilaterally symmetrical and a radiograph of the opposite foot may therefore prove misleading. A study of the bony architecture by means of a lens, however, will decide the issue. A condition resembling an apophysitis also occurs in these bones and may cause pain and disability so severe as to demand removal of the bone (see p. 436).

3.–INFECTIONS

(1)—Aetiology

524.] In approaching this subject it is impossible to avoid a comparison with infections of the hand (see HAND, DISEASES AND DEFORMITIES), for these have been more extensively studied, and the anatomical similarities of hand and foot suggest that knowledge obtained of the one might reasonably be applied to the other. While this is in general true, there are differences in the incidence and spread of infection which it is necessary to consider.

Incidence Although the functions of the foot are coarser and more onerous than those of the hand, infections are less common, for the prehensility which makes the hand so much more useful than the foot renders it

liable to the various injuries associated with manual work. The thick cornified layer of the skin of the sole, on the contrary, forms an effective barrier to minor penetrating wounds, and the enclosure of the foot in shoe or boot affords still further protection.

The common type of infection in the hands is that in which the organisms are directly introduced from without; in the foot infections are more usually intrinsic, arising from pathological structures such as bursae, blisters, and corns. The sites of origin and the planes of spread are thus different in the two extremities. Thus it is rare to find infection of the thecal sheaths or of the deep lymphatic spaces in the foot, both common sites in the hand.

The anatomical limits of these structures have, therefore, received less attention than they have been given, e.g. by Kanavel, in the hand. The ultimate results of infection too are less important economically, because interference with the function of the foot, although serious, is less disabling to the average wage-earner than a corresponding condition of the hand.

The increasing number of road accidents, however, is a factor tending to multiply the number of grossly infected contused wounds often affecting the deeper structures. In consequence it is now necessary to study the spread of infections in the foot as thoroughly as it has already been done in the hand.

(2)—Acute Infections

(a) Superficial Infections

Superficial lesions are seen chiefly in the thin skin of the dorsum and sides of the foot; rarely do they occur on the thick skin of the sole. Most of these conditions arise as a spread from an infected blister or bursa. The loose character of the skin in this situation leads to a well-marked inflammatory oedema; the whole dorsum of the foot becomes *Oedema* puffed up, and the depressions around the malleoli are obliterated. Such infections, if streptococcal, may be associated with lymphangitis, usually seen on the front and inner side of the leg, and with enlargement of the inguinal lymphatic glands. A septicaemia, not uncommonly fatal, is the most serious complication.

Oedema of the dorsum, however, is also met with in deep infections of the sole, and, as in the case of the hand, pus confined under the plantar fascia will make its way along the lumbrical tendons to the interdigital spaces or to the sides of the foot. Thrombosis of the superficial veins may accompany or be the origin of the infection.

Inflammation of the nail-bed usually arises from an ingrowing toe- *Inflammation* nail but occasionally is secondary to a subungual haematoma. The *of nail-bed* ordinary whitlow is rare; when infection of the theca does occur there is not a direct spread to the ankle region because, in contrast to the arrangement in the hand, none of the sheaths passes proximally farther than the middle of the metatarsal bones.

The bursae which more commonly become infected are those associated

*Infected
bursae*

with corns, the one over the head of the first metatarsal and those around the insertion of the tendo calcaneus (tendo Achillis). As the overlying skin is nearly always pathologically thickened, the infection is unable to reach the surface, and so spread in other directions is provoked.

(b) Deep Infections

*Plantar
fascia*

As there is so little tissue between the skin and the bones on the dorsum of the foot, a really deep-seated infection of the soft parts can be observed only in the sole. The fascial arrangements here must receive attention if the planes of spread are to be clearly understood. The skin is intimately attached to the plantar fascia, the movements of
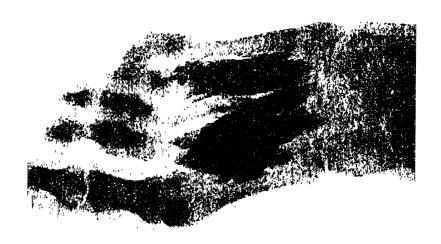
FIG. 99.—Radiograph after injections of lipiodol into chief plantar fascial spaces; these spaces correspond to the thenar and palmar spaces in hand

which it follows; only rarely can infection occur between the two. Two deep extensions from this fascia pass between the flexor brevis digitorum in the centre and the abductors of the hallux and little toe on the medial and lateral sides respectively. These extensions surround the long tendons and blend with the fascia covering the abductor muscles. The

*Three
superficial
compartments*

superficial musculature is thus divided into three fascial compartments. The central compartment extends forwards to the interdigital spaces and communicates with the dorsum around the lumbrical tendons. The medial and lateral compartments are continuous round the sides of the foot with the superficial fascial compartment on the dorsum, and when suppuration occurs in them the pus tracks to the sides of the foot, and here the maximum swelling and tenderness are found. The foot differs from the hand in the presence of these more superficial compartments owing to the additional intrinsic muscles.

The still deeper compartments are best demonstrated by special

methods. If iodized oil, e.g. lipiodol, is injected deeply into the meta- *Two deeper*
tarsal region a radiograph shows that the fascia covering the adductor *compartments*
muscles of the great toe divides the region into two main compartments
(see Fig. 99), which correspond exactly to the palmar and thenar com-
partments demonstrated by Kanavel in the hand. Pus in the deeper
compartments of the sole is more confined than that in the palmar
compartments and is unable so readily to track along the lumbrical
tendons; as, however, deep infection rarely occurs in the absence of a
penetrating wound, through which discharge naturally occurs, a state
of affairs corresponding to the 'Kanavel hand' is practically never
encountered. As the tendon sheaths are all discontinuous through the
sole, involvement of the sheaths around the ankle is unlikely, apart
from local penetrating injury.

(c) Infections of Joints and Bones

Although chronic affections of the joints of the foot are fairly common, *Aetiology*
acute suppurative infections are uncommon in the absence of injury.
Occasionally suppuration in the bursa over the head of the first meta-
tarsal bone spreads through the capsule into the underlying joint: this
applies also to the bursae associated with hammer-toe and corns.
Blood-borne streptococcal arthritis sometimes occurs in the ankle and
other joints, and a gonococcal invasion of the capsules of the tarsal
joints and the neighbouring ligaments and fasciae is a potent cause of
acute flat-foot.

Acute osteomyelitis of the tarsal and metatarsal bones is commoner *Acute*
than infection of joints and leads to all the classical signs and symptoms *osteomyelitis*
of the condition. The only bone of the tarsus having an ununited
epiphysis at the age when osteomyelitis is common is the calcaneus
(os calcis); for this reason both acute and chronic osteomyelitis occur
more often here than in the other bones.

A special feature of osteomyelitis of the tarsal bones is that the very
intimate connexions between them allow infection to spread readily
from one to its neighbours, and so several bones become involved in
the process. This is best demonstrated in a radiograph, but, even when
one bone alone is involved, the active hyperaemia induced causes a
wide-spread absorption of calcium salts which, by producing a diffuse
rarefaction in the radiograph, may be very misleading.

Pus arising from the bones tends to track under the deep fascia of the *Spread of pus*
dorsum and produce an extensive oedema, making localization of its
origin difficult. Such a collection spreads laterally and points on the
sides of the foot.

Gangrene of the toes and foot is associated with infection usually only *Gangrene*
when of the moist diabetic variety; the dry senile gangrene commonly
remains uninfected. Localized patches of infected gangrene due to
pressure are sometimes found behind the heel or over the malleoli. In
paralysed or bedridden patients they are produced by the mere weight
of the leg resting upon the heel; in other instances the pressure is due

to a badly fitting or improperly applied splint. The use of plaster splints without padding is particularly dangerous in this respect and needs special care in application and constant subsequent supervision.

Bacillary infections   In addition to the common coccal infections the foot is prone to infection with the *Bacterium coli*, the *Clostridium welchii*, and the *Clostridium tetani*. As in the latter two of these infections the prophylactic injection of antisera is of proved value this precaution should never be neglected in any penetrating injury.

(3)—Chronic Infections

Tuberculosis   Of the chronic infections of the foot tuberculosis is the commonest. For reasons given above the calcaneus (os calcis) is the most frequently involved of the tarsal bones, but in infancy tuberculous dactylitis may occur.

As in the acute cases, the infection may spread to surrounding bones and joints, causing a general invasion of the tarsus. Apart from bone infection tuberculosis affects the ankle joint (usually, however, secondarily to bone infection) and, rarely, the metatarsophalangeal joint of the great toe. Tuberculous synovitis is very uncommon in this region, although a 'rheumatic' tenosynovitis may occur.

Gonorrhoea   Gonorrhoea may cause a painful fasciitis of the sole or a periarthritis, and painful subacute nodules are sometimes the sequel of a generalized infection.

Syphilis   The sole of the foot is a common site of the secondary rashes of syphilis, but other syphilitic lesions, such as gummata, are rare in this region.

Enteric   Enteric fever occasionally causes a definite osteoperiostitis of the calcaneus (os calcis), but usually the painful heels which may follow this fever are, like those of influenza, due to renewed weight-bearing rather than to local infection.

(4)—Treatment

Cellulitis   As in other parts of the body, streptococcal cellulitis demands conservative treatment. The risk of opening up fresh areas to infection before the patient's general resistance is adequate and of causing septicaemia is so great that the older method of making multiple incisions to relieve tension is definitely hazardous.

In such cases the use of antitoxic sera and of chemotherapeutic agents of the sulphonamide group, e.g. prontosil and proseptasine, should be adopted until there is definite evidence of localization and pus formation (see p. 157). Thenceforth the case may be treated as any other infection. In true erysipelas the infection is so superficial that it is both logical and of proved value to use ultra-violet rays.

Incision   Incisions for drainage should be made in the foot on the lateral aspects, i.e. the positions to which natural drainage tends. Incisions through the sole should be avoided, not only to escape a scar in the area subject to pressure but also because deep pus can be reached only at

the expense of possible damage to the many structures in the sole. The
best incisions for dealing with infections of the toes are analogous to
those advocated by Kanavel for the fingers (see HAND, DISEASES AND
DEFORMITIES).

In particular, infection of the pulp under the terminal phalanx should
be treated by a horseshoe incision skirting the end of the toe, the whole
pulp being raised off the phalanx. Suppuration in a bursa under a corn
may often be drained by paring down the cornified layer until the
cavity is entered. For the larger and deeper bursae a proper incision is
necessary. In dealing with suppuration associated with an ingrowing
nail the most important point is to remove the small splinter of nail
which will be found to have penetrated the soft tissues in the lateral
nail-groove.

Acute osteomyelitis needs immediate drainage but, if localization is *Acute*
uncertain, it is sometimes better, provided the patient's condition *osteomyelitis*
allows, to wait a little rather than to endanger important structures by
exploratory dissection.

Tuberculous osteitis, in the absence of general contra-indications, *Tuberculosis*
often needs surgical intervention, which consists in thorough curettage
of the cavity, followed by packing with some such antiseptic as formalin
2 per cent in glycerin. General constitutional treatment and local rest
are as important here as in other regions and in many cases will be all
that is required, especially in the young. Tuberculosis of the ankle joint
is treated conservatively with good results, but in the adult, and
especially in the senile, sinuses are apt to form, and then the question
of amputation must seriously be considered.

4.–VERRUCA PEDIS

525.] The unique type of wart to which the above term is applied is
really a papilloma which, occurring on a weight-bearing area, becomes
depressed into the subcutaneous tissues and covered by a horny plate
resembling a callosity; it is, indeed, often wrongly diagnosed as a
callosity. These warts are infectious and inoculable and are thought to
be due to a filter-passing virus. They are painful and tender and vary
in size from a pin's head to half-a-crown. The commonest sites are the
metatarsal pads and the region in front of the heel pad, but no part of
the sole is immune. As might be expected from their nature, they are
not uncommonly multiple and tend to occur in adolescents with a moist
soft skin. The condition is prevalent in schools and may affect all the
occupants of dormitories.

The diagnosis is made by observing the tips of the papillae through *Diagnosis*
the translucent horny covering; this is best done by powerful trans-
illumination of the surroundings. Sometimes it is necessary to pare down
the horny layer before the characteristic appearance can be recognized;
when small haemorrhages have occurred into the tips of the papillae
as a result of trauma recognition is easier. Pain and tenderness in a

callosity should always arouse suspicion and, if the frequency of the condition is remembered, the diagnosis is straightforward.

Treatment   In the belief that the condition may be constitutional various internal medicaments have been used, but they are probably of little value.

Prophylaxis   Prophylaxis is particularly important when the disease breaks out in schools. It necessitates attention not only to foot-gear but also to such objects as bath mats, which often carry the infection from one individual to another. The use of thick paper and cardboard slippers, which can often be renewed, is advisable for patients in households in which other methods of prophylaxis would be difficult of application.

Local treatment   Various destructive agents are used in the treatment of the lesion, the rest of the foot being protected from implantation by the frequent application of any spirituous antiseptic, e.g. biniodide of mercury, 1 in 1,000. Freezing with solid carbon dioxide is the choice of some; others use the actual cautery. Electrolysis is a popular method, and scraping with a Volkmann's spoon under local anaesthesia is sometimes used by dermatologists. The chiropodist pares down the horny layer until the tips of the papillae are exposed and then applies a chemical caustic, e.g. nitric acid, monochloracetic acid, or silver nitrate, the application being repeated every three or four days.

Irradiation   A much more pleasant method of treatment is by a two- or three-pastille dose of X-rays or radium; in the latter case either the beta or the gamma rays may be used. These methods have the great advantage that they cause little discomfort or disability; the verruca usually disappears without more than a transient reaction. All affected areas should be treated at the same time so that there is no possibility of reinfection.

5.–PAINFUL CONDITIONS

(1)—Metatarsalgia

526.] This painful affection of the fore-part of the foot was first described by Morton, of Philadelphia, in 1876. He assumed that it was due to compression of the digital nerves as they pass between the heads of the metatarsal bones. Unfortunately there has been a tendency to describe any pain in the fore-part of the foot as metatarsalgia, although the true condition is not very common.

Clinical picture   Typically it occurs unilaterally in women; a preliminary burning or tingling sensation gradually develops and extends with much severe lancinating pain to the tips of the fourth and fifth toes, occasionally of the third or second toe. The pain occurs suddenly and compels the patient to remove the shoe, manipulate the toes, and squeeze the metatarsals together. The attacks occur with increasing frequency, until almost any attempt at walking becomes impossible. For many reasons it seems likely that the pain is developed not by lateral pressure on the nerves but by the abnormal pressure under the heads of the metatarsals in splay-foot.

Diagnosis   Before treatment is undertaken it is necessary to be quite sure of the diagnosis; other causes of pain in this region must be definitely excluded.

A radiograph will be of help in this respect and may reveal any undue prominence or enlargement of the metatarsal head, which may be acting as an aggravating factor.

Treatment is directed to the avoidance of pressure under the fourth *Treatment* metatarsal head. The chiropodist does this by fitting a pared pad of felt just below the head, and the splay-foot is supported by a metatarsal strap and by shoes having a snugly fitting instep. Supports made of leather, rubber, or metal may be incorporated in the shoe, but great care must be taken to see that they come in the correct position, behind and not under the head of the bone.

A metatarsal bar to the shoe gives rapid relief in this condition but must be continued for a long time, perhaps permanently. In exceptional cases excision of the head of the metatarsal may be practised and, if properly performed, leaves but slight weakness of the foot. If a secondary traumatic neuritis has developed, the nerve may either be avulsed or injected with alcohol. A pseudo-metatarsalgia of neurotic origin is difficult both to distinguish and to treat, but the fact that it does not yield to ordinary methods of treatment should arouse suspicion.

(2)—Painful Heels

Pain in the heel is met with under such various conditions that a summary only will be given here. Usually tenderness rather than spontaneous pain is the complaint, and a thorough investigation is necessary before any conclusion can be reached as to the cause. A change of *Due to* occupation to one involving much standing or walking is occasionally *change of occupation* to blame, the tissues not having time to respond to the increased 'hammering' to which they are now subjected. A mild traumatic peri- *To periostitis* ostitis results which is particularly resistant to any treatment other than rest. The painful heels which follow prolonged confinement to bed are of a similar nature; caution should be exercised in getting these patients on to their feet again. In some rare instances after an infective illness *To infective* there is a real infection of the bone or periosteum, which gives definite *illnesses* radiological changes. Even after influenza painful heels may result, but it is a moot point whether there is any actual infection present in these cases. Formerly a common cause was enteric fever, but with the diminishing incidence of this disease such cases are now uncommon. The acute flat-foot of gonorrhoea is associated with great tenderness *To gonococcal* under the heel; the extension of tenderness forwards, however, should *flat-foot* distinguish it. Pain under the heel in policemen and postmen (the *To bursitis* 'policeman's heel' of the States) is attributed to inflammation of a small bursa under the weight-bearing surface of the calcaneus (os calcis). Such a bursa is not described in this country, and it is probable that the condition is a localized periostitis. A very obvious cause of painful heel is *To bony spur* the development of a bony spur on the under aspect of the calcaneus *on os calcis* (os calcis) at the point of attachment of the plantar fascia. Here the tenderness is farther forward than in the other types; the diagnosis is established by radiography, but the fibrositis which precedes the develop-

ment of a spur may cause pain before the bony outgrowth can be demonstrated.

To infections of bone   Definite infections of the bone, such as osteomyelitis and tuberculosis, are uncommon causes of pain, and very rarely new growths may be responsible. In children an apophysitis and juxta-epiphysial strain have to be considered, the differentiation being easily made by radiography.

To apophysitis and strain

To oedema of fibro-adipose tissues   When the tenderness is over the back of the heel, bursitis is a common cause; in many such instances, however, the swelling is due to inflammatory oedema of the fibro-adipose tissues here rather than to fluid in a bursa. These cases often have circulatory disturbances in this situation and are prone to chilblains.

To other local causes   Excess of callus must not be overlooked, nor the blisters which follow the rub of boots or shoes. Gouty deposits in the heel-pad cause great disability and may need removal.

Referred pain in heel   Finally it must be borne in mind that pain in the heel may be referred from some lesion higher up the limb or even from a structure so remote as the bladder or the kidney.

Treatment   The treatment of painful heels must follow logically upon the diagnosis of the cause; it may vary from wearing a heel-pad of sponge rubber to an operation for the removal of a spur or bursa.

(3)—Osteochondritis and Apophysitis

These conditions, of unknown aetiology, are seen in the foot in connexion with the epiphysis of the calcaneus (os calcis), the navicular

FIG. 100.—Köhler's disease of scaphoid. The ossific nucleus is flattened, very dense, and fragmented

(scaphoid) (Köhler's disease, see EPIPHYSES, DISEASES AND INJURIES, p. 133), and, possibly, the head of the second metatarsal in Freiberg's

infraction. They are all probably similar in nature to pseudo-coxalgia and Schlatter's disease of the tuberosity (tubercle) of the tibia. They give rise to a slight aching pain in the affected region and to a limp after exertion and occur at an age when bone formation in the epiphyses is very active. Radiographically there is fragmentation of the bone with increased density and flattening of the ossific nuclei (see Fig. 100). The condition appears to be self-limiting (except Freiberg's disease) and needs little treatment other than rest and the relief of strain.

6.–TUMOURS

527.] Tumours of the foot are uncommon, but various types of chondromas, osteomas, fibromas, and lipomas occur without any features distinguishing them from such new growths found elsewhere. Squamous epithelioma and rodent ulcer rarely affect the skin, particularly of the dorsum of the foot, and osteogenic sarcoma is occasionally seen in the metatarsals. Melanoma deserves special mention because, in addition to starting in a pigmented mole on the dorsum, it may also grow from the nail-bed, especially that of the great toe. Its great importance lies in the fact that it is liable to be wrongly diagnosed as a subungual whitlow or a haematoma until the appearance of secondary growths in the inguinal glands or elsewhere reveals its true nature.

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FRACTURES

FRAGILITAS OSSIUM

FRAMBOESIA

FRECKLES

See Skin Tumours

FRIEDMAN'S TEST

See Pregnancy; *and* Sex Hormones

FRIEDREICH'S ATAXY

and Spinal Cord Diseases

FROST-BITE
AND TRENCH-FOOT

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Reference may also be made to the following titles:

CHILBLAINS   ERYTHROCYANOSIS
RAYNAUD'S DISEASE

1.–DEFINITIONS

528.] The terms frost-bite and trench-foot may not be accurate, descriptively or scientifically, but the nomenclature has become sanctioned by usage and, at least, conveys some explanation of the chief causal factors and environment.

Frost-bite and trench-foot are, pathologically, identical conditions due to the action of cold, varying in degree and contributory factors, whereby the tissues are wholly or in part deprived of their blood-supply. Cold is the main causal factor in frost-bite, whereas exposure to cold combined with wet and inactivity of the circulation caused by muscular inertia or mechanical constriction, produces the condition known as trench-foot. Technically, a vasomotor paresis passes on to paralysis with consequent haemostasis and oedema, and ultimately to gangrene. A reflex vasoconstrictive action is produced by cold, and the ischaemic state causes secondary nervous and trophic complications.

2.–AETIOLOGY

Cold, whether atmospheric or due to contact with frozen substances, *Critical*
is the sole causal factor of frost-bite and the main factor in the produc- *temperature*
tion of trench-foot. Cohnheim and Norman Lake showed that cold
below – 6 C. has very different effects on biological processes from cold
above – 6˙ C.: this temperature level should be regarded as a critical
threshold. Frost-bite is caused by fierce cold alone, though the action *Frost-bite*
of the cold is intensified by external conditions, wind and moisture on
the part affected. Trench-foot results from cold and wet plus muscular *Trench-foot*
and circulatory inertia; cold alone does not cause trench-foot; cold and
wet are not sufficient to cause it typically, muscular and circulatory
inertia being an essential factor. The lumber-men on the timber rafts
in Canada endure cold and wet for days on end, but they freely work
the muscles of the lower extremities and do not suffer from trench-foot,
which, during the Great War, caused such great wastage of man-power
among those who spent long hours in cramped positions in confined
spaces and were exposed to cold and wet. It is of more than historical
interest to note that Baron Larrey, in several phases of the Napoleonic
campaigns, remarked that the soldiers' feet suffered more severely when
the snow melted than when frost held the ground in a dry hard grip,
and that Larrey marched on foot during the disastrous retreat from
Moscow, having observed that many of those who rode contracted
gangrene of the feet when they warmed their half-frozen limbs at a fire.
Macpherson, during the Russo-Japanese War (1905), and Max Page in
the Balkans (1912), both recorded that a temperature above freezing
point was a factor producing the condition now known as trench-foot.
  In both frost-bite and trench-foot predisposing and contributory factors *Predisposing*
are hunger, exhaustion, malnutrition, debilitating diseases, and all cir- *and*
contributory
cumstances which lower vitality. Susceptibility is also a factor: subjects *factors*
of vasomotor instability, of 'angioneurotic disposition', or those who
have had previous attacks of frost-bite or allied conditions, are more
vulnerable than others. Natives of tropical and subtropical countries
who have not acquired a reasonable degree of acclimatization are natur-
ally more liable to suffer from cold and the effects of cold. During the
Great War French observers noted that their Senegalese troops were
more severely affected than the Moroccans, the Moroccans more than
the men of the Midi, and the men of the Midi more than the Bretons
and Normans.

3.–MORBID ANATOMY

In frost-bite and trench-foot the sequence of events is as follows: the *Sequence of*
arterioles become contracted practically to obliteration; the pressure in *events in*
vessels
the capillaries and veins is reduced to a minimum (the dead white
'syncope' phase); then the involuntary muscle-fibres in the walls of the

arterioles, having been tonically contracted for a considerable time, become paralysed and relax. The arterioles dilate enormously, the full arterial pressure is transmitted to the capillaries which cannot stand the strain, and through the capillary walls the fluids, or fluids and cells,

Exudate of the blood pass into the surrounding tissues. This exudate contains fibrinogen, the semi-solid fibrinous deposit accounting for the type of oedema, frequently noted in trench-foot, which does not pit on pressure. The exudate presses on the veins, and a vicious circle is set up; obstruction to the venous return increases the capillary pressure, the exudate is thus increased, and the increased exudate infiltrates adjoining structures, including muscles and nerves. The actual pressure of the exudate may so embarrass the blood-supply

Gangrene and return as to cause local gangrene (see Fig. 101).

In minor cases the necrosed tissue may be slowly absorbed; in more serious cases, when the part has suffered long exposure and the deeper tissues have become involved, sloughing of the necrosed tissue occurs. The description of

Histology the histology of trench-foot is almost entirely the work of Lorrain Smith, Ritchie, and Dawson; the

Blood- chief change is in the blood-vessels,
vessels which show dilatation of the lumen,

FIG. 101.—Ulceration of inner side of distal part of great toe by superficial gangrene of skin. (This and Figs. 102 and 103 from *Proceedings of the Royal Society of Medicine*, 1915)

swelling of the endothelium of the intima, and vacuolation in the muscular media. There is increase in the number of cells in the perivascular tissue. The lymphatic vessels are, in some cases, unaltered; in others they are filled with masses of cells and fibrin.

Tissue spaces In the tissue spaces the swelling and separation of the collagen bundles are very noticeable. In cases in which oedema has been present for some time there is abundant diffuse infiltration of the tissues with leucocytes. If the foot has been immersed in hot water there is, in addition, diffuse infiltration with red corpuscles, the damaged blood-vessels having given way under the strain of the additional congestion caused by warmth.

Voluntary The voluntary muscles exhibit loss of striation, and in cases of longer
muscles duration infiltration with leucocytes and a small deposit of fibrin between the muscular fibres.

Nerves The nerves show oedematous swelling of the axis-cylinders, this being
Lymph merely a part of the general oedema. The regional lymphatic glands are
glands enlarged from dilatation of the sinuses and hypertrophy of the follicles.

Sinuses The sinuses contain fibrin in the form of granules and threads; in the network formed by these may be found red cells, polymorphonuclears,

and proliferated endothelial cells, the endothelial cells being actively phagocytic for red cells and polymorphonuclears.

4.–CLINICAL PICTURE

In true frost-bite of the first degree the subject is usually conscious of a *First degree* pricking burning sensation in the part, which passes on to numbness and anaesthesia. The affected area is well-defined and white—a whiteness rather more waxy in colour but otherwise resembling the familiar appearance of the skin when ethyl chloride has been sprayed on as a local anaesthetic. The fingers and toes, when affected, cannot be moved. The onset is often so insidious that the subject may be unaware of the condition.

(a)   (b)
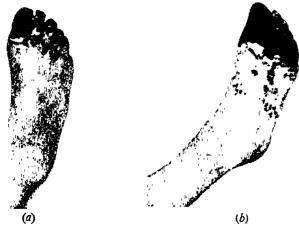
FIG. 102.—Dry gangrene. (*a*) Of four inner toes, great toe being most affected and rest of foot normal; (*b*) of anterior part of foot with subcutaneous haemorrhage under skin of dorsum of foot

This first stage of frost-bite, unless the circulation is restored, passes *Second degree* on to the second, in which the skin becomes pink, red and mottled with blue, and oedematous, and the clinical picture is to all intents and purposes identical with that of established trench-foot.

The onset of trench-foot is also often insidious. The patient may *Onset* complain only of coldness and numbness in his feet, though after the removal of the boots intense pain often accompanies the swelling which had been held in check by the constricting foot-gear. In the earlier stages *Appearance* the skin is white and swollen, but unless appropriate treatment is *of skin* adopted to restore the circulation this appearance alters and the skin becomes bluish-red in mottled patches or diffusely over the affected area. Blisters containing straw-coloured or blood-stained serum appear *Blisters* on the surface and break down with the production first of dark-brown or black crusts and later, as these separate from the necrosed underlying tissues, of ulcers. The toes may turn black and the nails become loosened *Toes* (see Fig. 102).

Pain   Pain may be extremely severe and call for morphine. Sensation is
always affected, and areas of anaesthesia and of paraesthesia may adjoin.

Necrosis   In more severe cases tissue necrosis extends below the deep fascia, and
and gangrene all stages of necrosis up to complete gangrene of the part may occur
but very seldom extend higher than the mid-tarsal joint. The illustration
(Fig. 103) shows the condition when, as happens in some cases, moist
gangrene sets in. Sloughing occurs rapidly, the foot becomes blackened,
there is extensive pus formation, the skin separates, and the tarsal and
metatarsal bones become infected.

(a)   (b)
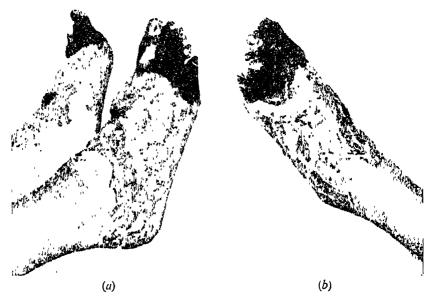
FIG. 103.—Moist gangrene. (a) In this case the process rapidly opened up the tendon
sheaths and tarsal joints, and severe toxic symptoms necessitated amputation
through lower third of leg on right side and through ankle joint on left; (b) in
this case there was rapid disorganization of tarsal joints and tetanus developed
on fourteenth day

Prognosis   In the absence of complications, such as sepsis or gas gangrene, and
according to the stage at which treatment is begun, the course towards
recovery of trench-foot is practically uneventful, reversing the morbid
changes which produced the condition; the absorption of the exudate,
the repair of damaged tissues, and the restoration of tone are matters
of time, rest, and treatment. In moderately severe cases the patient
remains unfit for military duty for a month, but in uncomplicated
cases the ultimate prognosis is good.

Sequelae   The principal sequelae, excluding loss of tissue varying from scarring to
the extreme of loss of toes or tarsal bones, are neuralgia, impairment of
sensation, and hyper-susceptibility to these symptoms if again exposed
to the causal factors and environment.

5.–DIFFERENTIAL DIAGNOSIS

Circumstantial evidence is in most cases sufficient to distinguish true *Differential incidence* frost-bite from trench-foot. Frost-bite is associated with arctic conditions, mountains and intense cold; trench-foot with a cold, wet, low-lying terrain: the wetness indicates that the cold is above freezing point, as otherwise the ground would be frozen hard. The onset of true frost-bite is manifested by rapid and complete loss of vitality through the whole thickness of the part: that of trench-foot is more insidious. Frost- *Parts of body attacked* bite attacks the face, nose, ears, chin (parts where the skin is stretched over bone and cartilage and has a comparatively attenuated blood-supply), the fingers, toes, and heels: whereas in trench-foot the area affected is not so limited, and the condition is very rare in parts other than the lower extremity.

Trench-foot has been compared with Raynaud's disease, but the *Diagnosis from Raynaud's disease* history of the angioneurotic disposition should be sufficient to prevent any confusion in diagnosis.

Chilblains are distinguished clinically by the intense itching compared *From chilblains* with the pain and anaesthesia of the condition under discussion, by the site of the chilblain, and by the circumscribed erythema.

6.–TREATMENT
(1)—Preventive

The factors predisposing to frost-bite must as far as possible be elim- *Frost-bite* inated and the general health and vigorous circulation maintained. Suitable cothing is of the greatest importance; it is necessary to ensure a non-conducting air-space between the skin and the cold atmospheric air. The clothing must be loose-fitting and without constricting bands and fastenings. Moisture from without and from within (perspiration) is harmful, because it produces a sodden condition of the skin and is a conductor of cold. Foot-gear presents the greatest difficulty: it is of the utmost importance to change wet socks and to rub the feet thoroughly dry before putting on dry socks. Boots should be roomy enough to allow of wearing two or even three pairs of socks without constricting the foot. Soft paraffin may be useful in protecting the face against wind, but grease as a prophylactic against frost-bite is not advisable.

In trench-foot as in frost-bite it is very important to eliminate as far as *Trench-foot* possible the predisposing factors, and the general rules as regards cloth-ing are the same. As wet plays such an important part in the causation, *Boots* most careful attention must be paid to boots, which should be roomy, not tightly laced, and kept under constant supervision so as to obtain repairs directly they are needed. The value of waders and gum-boots is doubtful unless the water is above the ankles, and then they are helpful only if they can be worn on dry feet and for short shifts; in such imperme-able coverings the feet perspire more than normally, and the skin becomes macerated. Puttees and garters must not be worn: they shrink in situ as

they become wet and constrict the limb. Whale-oil and goose-grease,
well rubbed into the feet, were, during the Great War, found of use in
preventing heat loss and in resisting the wet factor; but there must be
facilities for washing off such applications after twenty-four hours,
otherwise they become objectionable and aggravate maceration. Raised
platforms and duck-boards are of use when the ground is merely muddy;
and, unless the ground is actually under water, skipping and stamping
exercises and flexion and extension of the toes inside the boots combat
the muscular inertia which plays such an important part in the causation.
Hot food and drink while the men are in the cold wet confined spaces
are obviously potent methods of increasing the resistance of the in-
dividual. Men exposed to the causal factors should not be allowed to
warm their feet by placing them near stoves or braziers.

(2)—Specific

Medical
Frost-bite of the first degree is treated by gentle friction sufficient to
restore the circulation; rubbing snow on the affected part is widely
advocated and used; the therapeutic value of snow in this connexion—
a hard-dying fetish—is difficult to assess. The treatment of frost-bite
after the first degree and of trench-foot will be discussed together, as
they are then practically identical conditions. Not on any account should
the affected part be exposed to warmth above the ward temperature and
tepid water only must be used for cleansing the feet preparatory to
treatment.

*Tetanus
antitoxin*
Tetanus antitoxin, 1,000 units, should be injected in every case, and
this dose should be repeated every six to seven days as long as breach of
surface exists. During the Great War the tetanus bacillus (*Clostridium
tetani*) developed in feet which did not show any obvious breach of
surface, having presumably entered through the fissures and rhagades
of macerated skin.

The aims of treatment are to assist the absorption of the exudate, to
restore the vessel walls, to clear the lymphatic paths, and to enable the
tissues which have suffered from infiltration to regain tone. Rest,
comfort, sleep, and good food are vitally important.

*Local
treatment*
The local treatment here advocated is one of several tried on a large
scale during the War and is now recommended because it gave better
results than control methods. As routine treatment it can be carried out
on a large scale and by comparatively unskilled attendants. With the
patient at absolute rest, the affected part is thoroughly cleansed in tepid
water with a soap composed of:

Powdered camphor – – – –	25 grams
Powdered borax – – – –	100 grams
Soft potash soap – – –	– to 1,000 grams

After washing and drying, a compress is applied soaked in:

Camphor – – – – –	1 gram
Borax – – – – –	15 grams
Sterile water – – –	– to 1,000 c.c.

It is gently squeezed, leaving the dressing quite moist, and applied over the whole area, which is then covered with cotton-wool and very lightly bandaged; this compress is changed every day until the swelling has subsided, usually in about a week in a case uncomplicated by blisters. The feet are then powdered and wrapped in dry cotton-wool. the patient being still kept at rest, for four or five days. Blisters, if present, are cut away with fine-pointed scissors, and the base is gently swabbed and covered with:

Camphor	–	–	–	–	30 grams
Ether	–	–	–	–	– to 1,000 c.c.

on a few layers of plain gauze, the compress being applied over this. If the discharge from the open surface is purulent, the area is dressed with Dakin's solution for the time required to clean up the surface. Separating sloughs should be left to come away without interference. The hard black firmly-attached dry patches of necrosed tissue may be scarified sufficiently to allow the camphor-ether solution to reach the underlying surface, and the patches to become loosened as sloughs. The shallow ulcers left after separation of the sloughs do not fail to respond to the camphor treatment nor become callous and indolent.

The local application is often effective in relieving pain. but in many *Morphine* cases the pain, particularly at night, is so terribly severe that morphine is necessary. Potassium iodide, 8 grains three times a day, for three or four days, is of great value in the routine treatment of pain in these cases.

Surgical intervention may be necessary for the removal of dead tissue, *Surgical* and partial amputations are sometimes required, but the surgical treatment of trench-foot is conservative, and the advice to surgeons in future wars may well be to leave the foot alone. The prognosis is invariably better than would seem possible from the first examinations of the discoloured foot with blebs and black areas of necrosis. The site of any operation ultimately necessary will define itself, and amputation is very seldom required higher than the mid-tarsal joint. Severe secondary infections, such as gas gangrene. pass out of the trench-foot category.

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FUNGOUS DISEASES

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Reference may also be made to the following titles:

ACTINOMYCOSIS   MYCETOMA

ALOPECIA   MYCOSIS FUNGOIDES

ASPERGILLOSIS   RHINOSPORIDIOSIS

BLASTOMYCOSIS   TORULOSIS

HAIR FOLLICLES, ABNOR-
  MALITIES AND DISEASES

I.—RINGWORM INFECTIONS

1.—DEFINITION

529.] Under this term are included those disorders that are caused by pathogenic *fungi imperfecti* of the family Gymnoascales.

2.—AETIOLOGY AND PATHOLOGY

Morphology   These fungi are composed of segmented mycelium, the short segments forming naked spores. In the skin the spores become elongated into new mycelial threads, which in their turn break up again into spores. Their aerobic method of proliferation is by means of aerial hyphae with terminal and lateral buds.

Habitat   Some of them are found only on the human skin; but a considerable number occur in the lower animals and can be transmitted to man. The animals from which infection most commonly takes place in England are cats, dogs, horses, and cattle. Those derived from animals generally produce a greater inflammatory reaction.

Classification   The differentiation of individual species and their nomenclature are very confused. For clinical purposes it is still most practical to retain the names in Sabouraud's classical treatise.

Biology   The prevalent species vary enormously according to geographical locality. Fungi can survive for a long time on common substances of vegetable or animal composition, but extensive investigations afford no evidence that ringworm fungi vegetate harmlessly on the healthy human skin. They may, however, be present in profusion in the hairs of animals without causing any clinical lesion. No organs other than the skin are attacked, although the fungi frequently enter the blood-stream.

3.–RINGWORM OF THE SCALP

(Synon. m.—Tinea capitis; tinea tonsurans)

(1)—Aetiology

Microsporosis

530.] Microsporosis is due to invasion of the hair-follicles by one of a *Varieties of*
number of varieties of ringworm fungi characterized by small spores, *microspora*
which form a mosaic-like sheath around the shaft. In England the great
majority of cases are due to *Microsporon audouini*, which apparently
only attacks human beings. A small proportion in England, but a much
larger percentage in America, are caused by other varieties, e.g. *M.
lanosum*, which can be transmitted from dogs and less often from cats,
M. felineum from cats, and *M. quinckeanum* from mice and occasionally
from horses. The animal microspora cause a greater degree of inflamma-
tion, even amounting to kerion. Microsporosis affects children from an
early age up till puberty, at which period the natural changes in the
skin lead to its spontaneous cure. It is contracted by direct contact or
by the medium of caps, hair-brushes, and the like, the incubation period
being three to eight days.

Trichophytosis

Trichophytosis occasionally affects adults as well as children. While
rather rare in England it is commoner on the Continent than micro-
sporosis. It is caused by a genus of fungi which in infected hairs form
chains of spore-like elements. In most trichophyta these are larger than
those of the microspora. There are two chief groups of species: (i) *Endothrix*
endothrix trichophyta are found only inside the fully infected hair *trichophyta*
(although in the early stages of invasion a few filaments can also be seen
outside) and are believed to be peculiar to man and to birds; (ii) ecto- *Ectothrix*
thrix or ectoendothrix trichophyta proliferate outside as well as inside *trichophyta*
the fully infected hair. They normally attack animals, especially horses
and cattle. If communicated to man they usually cause kerion.

Kerion

Kerion is generally of animal origin and caused by *T. ectoendothrix*
or, more rarely, by microspora. It may occur at any age and is the
commonest variety of scalp ringworm in adults.

(2)—Clinical Picture

Microsporosis

Within circumscribed, rather well-defined, generally round areas the
hair falls out, or rather breaks off close to the skin, leaving little stumps,
which look greyish or frosted, are often bent or split, and, having lost
their elasticity, point in different directions. The skin between them is
scaly. The earliest sign of infection is a small pinkish macule or scaly *Progress of*
patch, most marked at the orifices of the hair-follicles. As a rule, several *lesions*

such foci coalesce and may involve the greater part of the scalp. Except occasionally in infants, the lesions do not clear up in the centre to form rings. Sometimes less well-defined lesions occur, with faint scaling and partial alopecia, gradually shading off into the normal scalp.

Trichophytosis

Appearances of lesions   Small scaly patches, roundish or irregular in outline, generally not larger than about 1 sq. cm., are found either solitary or disseminated in large numbers over the scalp. Stumps are much scarcer than in microsporosis, the affected hairs more often breaking off at the follicular orifices, in which they may be seen as black dots. Stumps, when present, may be white and opaque or resemble short atrophic hairs; they are irregularly distributed, singly or in small groups, among healthy hairs. The surrounding follicles may have the appearance of goose-flesh.

Kerion

This is a well-defined, generally round, boggy red swelling, dotted over with small perifollicular abscesses exuding sero-pus, in the centre of which a loose hair can generally be detected and between which are a few opaque stumps. The diameter varies from 1 cm. to 5 cm. or more. As a rule there is only a solitary lesion, but there may be several. Kerion represents an acute inflammatory reaction to the fungus. (See Fig. 104.)

FIG. 104.—Kerion
(Photograph kindly lent by Dr. J. T. Ingram)

(3)—Prognosis

Microsporosis

Microsporosis is exceedingly contagious in children. It persists and extends, if untreated, until puberty; then it spontaneously dies out. In the rare cases in which the response to infection is very inflammatory or suppurative spontaneous cure may take place earlier. An attack does not confer immunity.

Trichophytosis

Trichophytosis is liable to persist indefinitely, even after puberty. Endothrix ringworm is particularly likely to be of long duration, owing to the difficulty in recognizing it. Ectothrix infections, which generally approach the kerion type, may disappear spontaneously.

Kerion

Owing to the intense local defensive reaction as well as to a general allergic response, kerion leads to a relatively rapid destruction of the fungi. Moreover, the follicular suppuration causes a spontaneous epilation: consequently kerion usually cures itself. The red bald patch which follows may last for six months or longer before the hair grows again, or there may even be some degree of permanent cicatricial baldness.

(4)—Diagnosis and Differential Diagnosis

Wood's light affords great assistance in the recognition of micro- *Wood's* sporosis. It is composed of long-wave ultra-violet rays, obtained by *light* filtering the rays from a mercury-vapour lamp through nickel oxide glass, whereby the luminous rays are cut off. Viewed by Wood's light in a dark room, hairs infected with microsporosis fluoresce a brilliant green. A single infected stump can thereby be very easily picked out from the rest of the hairs. The method is of particular value after epilation, in making sure that cure is complete, and for routine inspection in schools. The hairs of cats infected with microsporosis exhibit the same green fluorescence. Very rarely microsporotic stumps fail to fluoresce. Hairs infected with the trichophyta do not give this green fluorescence but may have a pale bluish sheen like that given by human epidermal scales and nails.

The final clinching of the diagnosis depends on demonstration of the *Demonstra-* fungus. A few stumps, placed in a drop of xylol on a slide under a *tion of fungus* *in stumps* cover-slip, should be examined microscopically with the ⅙ inch objective.

Microsporon can be recognized as a mosaic of polygonal spores of *Micro-* uniform size forming a sheath round the hair-shaft. Sometimes mycelial *sporosis* threads can be seen inside the shaft. In the black-dot ringworm caused *Endothrix* by endothrix one may need a needle or comedo-expressor to get out the stumps, which are often found curled up under a scale; but endothrix may be found in hairs half an inch or even more in length and is recognized as chains of large spores inside the shaft.

In kerion the stumps are easily pulled out and under the microscope *Kerion* present mycelial threads and chains of spores around and within them. The fungus is most likely to be found in the stumps just within the peripheral scaly fringe.

(i) Seborrhoeic dermatitis sometimes produces closely similar scaling *Diagnosis* but, as a rule, affects the greater part of the scalp fairly evenly. Stumps *from* *seborrhoeic* do not occur. It is therefore endothrix infections, in which stumps are *dermatitis* few and individual patches ill-defined, that are most likely to be taken for seborrhoeic dermatitis.

(ii) Psoriasis produces silvery scales, piled up in a lamellar arrangement *From* and sharply circumscribed with a red border; falling of the hair is ex- *psoriasis* ceptional and there are no stumps.

(iii) In alopecia areata the skin within the bald patches is smooth, *From* *alopecia* devoid of scaling and of the same colour as the surrounding skin. *areata*

Stumps, if present, have a characteristic exclamation-mark shape from thinning and depigmentation of the attached end.

From staphylo-coccal folliculitis

(iv) Staphylococcal folliculitis may resemble kerion but does not form such sharply demarcated clusters of pustules or have such an infiltrated boggy base.

(5)—Treatment

When a case has occurred, all contacts, e.g. the rest of a school, must be carefully searched.

Fomentations for suppurative forms

For suppurative ringworms, with their tendency to spontaneous cure, X-rays are not only unnecessary but injurious. It is best to hasten the natural process by fomenting with 1 part of mercury biniodide in 4,000 parts of physiological saline. The rest of the scalp should be anointed with Whitfield's compound benzoic acid ointment B.P.C., to protect it from inoculation.

Animal microspora

G. M. Lewis states that infections with animal microspora, even if non-suppurative, can be cured in three to twelve weeks without epilation. The local treatment recommended by him consists of the application of an ointment of iodine, thymol, oil of cinnamon, 1 per cent of each in soft paraffin, twice daily after washing with soap and water. Animal microsporosis, however, can only be distinguished by culture and the opinion of an experienced mycologist.

Epilation

All other kinds of ringworm of the scalp can only be eradicated by making all the hair fall out completely, which can be achieved by either X-rays or thallium.

X-rays

X-rays are the better method when a suitable apparatus and an expert operator are available, but they should not be used in the presence of inflammation or pyococcal infection or if the hair has not completely regrown after a previous X-ray treatment. The hair should previously be clipped short. Children even as young as one year can be subjected to the action of X-rays, but for those under four years of age a special immobilizing apparatus is generally needed. If this is not available, sedatives, such as chloral hydrate and potassium bromide, for a day or two beforehand may quieten them enough.

About eighteen days after the treatment the hair becomes loose; it should all have fallen out by the end of the fourth week. If at the end of a further month infected hairs cannot be discovered either by Wood's light or microscopically, the child may be considered cured. The hair generally begins to grow again about three months after the treatment.

During the whole period from diagnosis till complete epilation the head should be washed once a day with soap and water, rubbed dry, in which process loose stumps are removed, and then covered with Whitfield's ointment. The child must wear a cotton cap made to fit closely and cover the whole of the hair. This should never be removed except to change it for a clean one or for purposes of treatment. These measures are to minimize the risk of dissemination or reinfection by contaminating pillows, hats, and the like.

If some of the infected stumps fail to be loosened by the X-rays, it is *Procedure if* best to get them out by producing a folliculitis, which should be serous *X-rays fail* and oedematous rather than purulent. Croton oil is perhaps the most *Croton oil* effective agent. If many stumps remain, the croton oil can be used in the form of an ointment, e.g. 10 per cent or more in equal parts of lanolin and soft paraffin, or, as a paint, dissolved in turpentine. Isolated stumps can be dealt with by dipping the eye of a size-16 sewing-needle in croton *Needling* oil and passing it, eye first, down the hair-follicle. These treatments are continued daily until the infected stumps (recognized by Wood's light if microsporic) are so loosened that they can be easily withdrawn by epilation-forceps without breaking. After needling, the stumps can sometimes be so withdrawn within a few minutes. The rest of the scalp should be protected with Whitfield's ointment. If, owing to inadequate dosage, epilation has quite failed over large areas, the X-rays may be repeated, but not before three months have elapsed since the preceding dose and only if the hair is growing well over the whole scalp.

The oral administration of thallium acetate offers a valuable alterna- *Thallium* tive to X-rays when these and an expert operator are not available, when they have been used unsuccessfully, or when the scalp is inflamed. Although grossly excessive or repeated doses are extremely dangerous and may even be fatal, there is little risk if the drug is accurately and properly administered. Many patients, however, complain of quite tem- porary anorexia, malaise, pains in the legs and feet, and occasionally drowsiness and muscular weakness.

The following is a summary of a routine which Ingram finds successful *Method of* in over 90 per cent of cases and perfectly safe. After clinical examination *administra-* and test of the urine, which must be free from albumin, the child is *tion* weighed naked. The weight in pounds multiplied by four gives the re- quired dose in milligrams. This is equivalent to a dose of 8·8 milligrams per kilogram of body-weight. More than 250 milligrams are never administered. The average age requiring 250 milligrams is nine years, up to which, therefore, there is little danger. Errors in dispensing may arise from the use of solutions of the drug. Tablets of various strengths can be made in different colours to be swallowed by the child with a drink of water.

Epilation generally begins about the eleventh to the fourteenth day. It is necessary to remove all the stumps quickly, as the new hair begins to grow after three weeks. To achieve this, Ingram recommends clipping *Painting with* the hair quite short and painting the scalp three times every day from *iodine* the onset of the treatment with 2 per cent solution of iodine. This leads to a coarse desquamation which reaches its height towards the end of the third week. Washing should be avoided for the first two weeks; but the scalp is washed about the seventeenth day, to loosen the desquama- tion, and again on the twenty-first, when most of the scales come away. After that it may be washed about once a week. Painting with the solu- tion of iodine is continued till all infected stumps have disappeared. This usually happens about nine weeks from the beginning of treatment.

If the iodine is carefully kept away from the forehead, the nape of the neck, and the retro-auricular folds, it does not cause serious discomfort and never, in Ingram's experience, provokes eczema. It is wise, however, to omit it for twenty-four hours after washing. If this treatment fails it is unwise to repeat it. Thallium salicylate has been found by Peli to be less toxic than the acetate, while having the same epilating power.

X-rays and thallium combined   The dangers of overdosage of thallium and of X-rays can be lessened by combining the two methods, two-thirds of an epilating dose of X-rays being followed a week later by two-thirds of the epilating dose of thallium; but the results are a little less certain.

4.–RINGWORM OF THE BEARD

(*Synonyms.*—Tinea barbae; tinea sycosis)

(1)—Aetiology

531.] The flat scaly type (see Clinical Picture) is generally due to an endothrix trichophyton; this, being almost confined to man, is usually conveyed by a barber's infected shaving-brush. The incubation period is four to five days. Occasionally an animal microsporon is to blame. The suppurative type is due to ectothrix trichophyta of animal origin and therefore most often attacks grooms and cattle-men.

(2)—Clinical Picture

Flat scaly form   There are two principal forms of ringworm of the beard: (i) the flat scaly form, which appears as round or ringed dry scaly reddish patches, within which the infected hairs break off, either leaving pale lustreless stumps, or so short as only to show as dark plugs in the pilosebaceous *Suppurative form*   orifices; and (ii) the suppurative form, in which aggregated groups of red papulo-pustules or nodules surround a number of hairs, there being some crusts of exuded serum. Infiltration may be massive enough to produce very large purplish lumps. Tinea rarely affects the upper lip. (See Fig. 105.)

(3)—Diagnosis and Differential Diagnosis

Microscopical demonstration of fungus   The diagnosis is made by demonstration of the fungus in the hairs, as described under ringworm of the scalp (see p. 453). Hairs should be chosen from the periphery of the lesion, and it may be necessary to examine a large number of them. In the flat scaly type mycelium may also be found in the scales (see p. 459).

Diagnosis from seborrhoeic pityriasis and eczema   The flat scaly form may be confused with seborrhoeic pityriasis or with scaly eczema; but these generally extend beyond the beard area, are not so distinctly circinate, and do not present stumps.

The suppurative form should be distinguished from staphylococcal sycosis, in the first place by the aggregation in groups of nodose infiltra-

tions and secondly by the presence of stumps and, often, small scaly *From* areas, in both of which the fungus can be found microscopically. In *staphylo-coccal* staphylococcal sycosis the upper lip is frequently involved. Acne vulgaris, *sycosis* essentially a disorder of adolescence, is distinguished by the presence of *From acne* comedones and by not being confined to the beard region. Bromides *vulgaris* and iodides may produce infiltrated pustular kerion-like lesions, closely resembling the suppurative form (see DRUG ERUPTIONS, Vol. IV, p. 261). *From drug* They may be distinguishable by other symptoms, such as coryza, or by *rashes* detecting the drug in the urine.

The framboesiform variety of secondary syphilis, consisting of fungating or vegetating plaques covered with crusts, can easily be mistaken for the suppurative form; but the lesions are not confined to the beard area.

From syphilis

(4)—Treatment

The flat scaly form if untreated persists indefinitely and is resistant to fungicidal applications. It is best to procure epilation with X-rays, after which the skin should be washed daily and anointed with dilute ammoniated mercury ointment. Croton oil must not be used except by needling. If X-rays are not available, an attempt should

Epilation
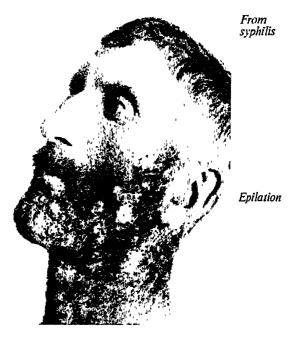
FIG. 105.—Tinea barbae contracted from a horse

(Photograph kindly lent by Dr. M. S. Thomson)

be made to epilate manually and apply a fungicidal ointment, such as Whitfield's ointment; the rest of the beard must be kept clipped short. In the suppurative form, which is more amenable, X-rays are contra-indicated. The best local treatment is to foment with a solu- *Fomentations* tion of mercury biniodide 1 part in 4,000 parts of physiological *and internal* saline. Jacobson (1932) recommended intramuscular injections of *treatment* sterile milk 5 to 10 c.c. every five days. Ravaut (1921) recommended daily intravenous injections of Lugol's iodine solution, beginning with 1 c.c. in 5 c.c. of distilled water and increasing by 1 c.c. daily till 5 c.c. are injected in 15 c.c. of distilled water. The maximum dose may be continued for two weeks. Gradually increasing intracutaneous injections of trichophytin or clasovaccine (Jausion and Sohier) may hasten cure.

5.—RINGWORM OF THE NAILS

(*Synonyms.*—Onychomycosis; tinea unguium)

(1)—Aetiology

532.] Ringworm of the nails is relatively rare in England but common in semi-tropical countries, especially in the Far East. It has been observed in several members of a family and in more than one generation. It is due either to a trichophyton or to the *Epidermophyton inguinale*.

(2)—Clinical Picture

Infection beneath free edge

Ringworm of the nail-plate generally begins beneath the free edge, where it heaps up friable horny material between the nail-bed and the nail-plate, which are thereby forced apart. The plate is subsequently invaded and becomes discoloured, thickened, mis-shapen, and brittle. One, several, or all the nails of one or both hands or feet may be attacked.

Infection from nail-fold

More rarely the infection starts from the nail-fold, whence it attacks the matrix. The nutrition of the nails is thereby interfered with, the lunule first becoming discoloured, depressed, and corrugated.

(3)—Diagnosis and Differential Diagnosis

Demonstration of fungus

A certain diagnosis can only be established by finding the fungus. Shavings of the nail-plate should be obtained with the edge of a broken glass slide and some of the inner ones left to soak in potassium hydroxide solution 30 per cent for several hours till they can be spread out in a thin smear under a cover-slip. They are then searched under high power for the presence of mycelial threads. (See p. 459.)

Differential diagnosis

The condition may be confused with eczema, in which, however, the surrounding skin is involved; with tertiary or congenital syphilis; or, most easily, with psoriasis. The free edge is apt to be more friable and shaggy than in any of these.

(4)—Treatment

Ringworm of the nails generally lasts many years and is singularly difficult to cure. A small proportion of cases are cured rapidly after a course of fractional or sub-intensive doses of X-rays, and this is worth a trial before proceeding to less pleasant measures.

X-rays

Fungicides

Mild cases may be cured by scraping down the nail as thin as possible with glass or a file or an electrically driven burr, and keeping it tied up with a fungicide, of which one of the most effective is Castellani's fuchsin paint, made in the following way. Mix saturated alcoholic solution of basic fuchsin 10 c.c., and 5 per cent phenol solution 100 c.c.; filter and add boric acid 1 gram; after two hours add acetone 5 c.c.; two hours later add resorcinol 10 grams. Dispense in a dark-coloured bottle with a glass stopper. Other effective fungicides are Whitfield's ointment,

iodine 1 per cent in alcohol or benzene, and saturated solution of chrysa-
robin in chloroform.

In more severe cases it is necessary to remove the nail-plate, to curette *Intractable*
the nail-bed thoroughly, and to dress the raw area continuously with a *cases*
fungicide; but even then the new nail is often found to be still infected,
and the nails and matrices must be extirpated, after which, of course,
the nails do not grow again.

6.–RINGWORM OF THE SMOOTH SKIN

(1)—Aetiology

533.] The macular lesions are commoner in children than in adults and
are often present about the face and neck in association with ringworm
of the scalp. The majority are caused by *M. audouini*. Circinate ring-
worm is also generally
due to a microsporon. It
attacks adults as well as
children and may be
caught from a cat or dog.
The plaques and vesico-
pustular lesions are, as a
rule, of trichophytic origin.

(2)—Clinical Picture

On the smooth skin, other
than the flexures and inter-
digital spaces, the lesions
are usually seen as round

FIG. 106.—Vesicular ringworm contracted from
a mouse

(Photograph kindly lent by Dr. J. T. Ingram)

patches which spread peripherally, healing in the centre so as to form
rings (tinea circinata). They are pale red and scaly and occasionally
vesicular or pustular (see Fig. 106). At any given moment they may
appear as scaly macules or plaques, ringed or gyrate figures, vesicular
or pustular patches, and occasionally as suppurative conglomerate
granulomatous nodules.

(3)—Diagnosis and Differential Diagnosis

Diagnosis is settled by the demonstration of the fungus in the scales. *Demonstra-*
A scraping is made with a scalpel from the border of a lesion moistened *tion of*
with a 20 per cent solution of potassium hydroxide; this is spread on *scales*
a slide, another drop of 20 per cent potassium hydroxide solution added,
and a cover-slip applied. When the material has soaked long enough
to be pressed out into a thin film, the outlines of the epidermic cells are
seen, under a $\frac{1}{6}$ inch objective and a small stop, to form a pattern like
wire-netting. Mycelium is detected as wavy branching refractile threads
cutting across this network.

Ringworm of the smooth skin must be distinguished from seborrhoeic

dermatitis, in which the scales are more yellowish and greasy; from psoriasis, in which the scales are laminated and silvery and the lesions more sharply defined; from pityriasis rosea, in which the herald patch may be extraordinarily similar but is followed by a profuse eruption of pale oval lesions bearing only a thin circular fringe of scales; and from discoid eczema. The ringed forms must also be distinguished from impetigo circinata, the edge of which is, however, composed of a continuous tubular blister; and from the very superficial form of tertiary syphilis.

(4)—Treatment

Cure is easily achieved by rubbing in Whitfield's ointment twice daily. It can occasionally be cured in one session by scrubbing with a piece of cotton-wool dipped in 3 per cent silver nitrate solution and then painting with weak solution of iodine.

7.–RINGWORM OF THE FLEXURES

(*Synonyms.*—Tinea cruris vel axillaris; epidermophytosis inguinalis; eczema marginatum; dhobie itch)

(1)—Aetiology

534.] Ringworm of the flexures is caused by the *Epidermophyton inguinale*, which is of human origin, growing in the superficial layers of the epidermis. It has become extremely common, especially in males, and can be caught by direct contact or from infected clothes or lavatory seats; but probably most often it is transferred from the toes. The incubation period is four days (Whitfield).

(2)—Clinical Picture

*Progress of
lesions*
In the groins, the commonest site, red maculo-papules spread and coalesce to form a red partially denuded patch, which gradually advances down the inner aspect of the thighs and, to a smaller extent, to the scrotum or labia and abdomen and sometimes the perineum and internatal cleft. The advancing border is generally deeper red than the old portions which are clearing up and is sharply demarcated by a scaly fringe. In severe cases it may be vesicular or pustular. The axillae and the submammary folds may be similarly involved. Sometimes painful fissures develop along the bottom of the folds. Itching may be intense and lead to scratching and consequent eczematization or secondary infection. The condition is worst in hot weather and may become inconspicuous and dormant in the winter.

(3)—Diagnosis and Differential Diagnosis

Diagnosis is established by finding the fungus in the peripheral scales (see p. 459). The spaces between the toes must also be searched.

The differential diagnosis is from seborrhoeic dermatitis, which gener- *Differential*
ally affects the scalp, face, or trunk as well; from intertrigo, which is *diagnosis*
more symmetrically disposed around a fold and more inflamed at the
centre than the edge; and from flexural psoriasis, which has a deeper
red and more raw appearance.

(4)—Treatment

The underclothes must be made of material which may be boiled, such
as cotton, and changed frequently. On no account must trousers or
breeches be worn next to the skin. The average case yields to the in-
unction twice daily of Whitfield's ointment. In very inflamed cases, in
which this may not be tolerated at first, treatment must begin with a
lotion, such as potassium permanganate 1 in 4,000 or monsol 1 in 500
of water. Such patients should lie up. If Whitfield's ointment is in-
effective or badly tolerated, it is best to paint the areas once daily with
Castellani's fuchsin paint; blisters should be pricked and the loose skin
snipped off beforehand. Treatment should be continued for a week or
two after apparent cure. The toes, if involved, must be dealt with at
the same time.

8.–RINGWORM OF THE FEET AND HANDS

(*Synonyms.*—Tinea interdigitalis; mango toe; Hongkong foot;
athlete's foot)

(1)—Aetiology

535.] The lesions, resembling those described under ringworm of the
smooth skin, have the same aetiology. The three principal forms are
caused by the *Epidermophyton inguinale* or the *Trichophyton (Epidermo-
phyton) interdigitale*. The disease is extremely common, especially in
the more well-to-do classes, and is probably transferred from one person
to another chiefly by bath-mats and wet changing-room floors. The
activity of the infection is favoured by heat and perhaps by alkaline
decomposition of accumulated sweat.

(2)—Clinical Picture

Besides the occasional occurrence of lesions similar to those described
under ringworm of the smooth skin, there are three principal forms.

Intertriginous

Between and underneath the toes, especially in the two outer inter-
digital spaces, the skin becomes sodden, looks opaque white, and peels
off to leave painful red sores; deep cracks may develop. This is the
commonest form. (See Fig. 107.)

Vesicular

There is a localized eruption of deeply set vesicles, especially on the
hollow of the soles and more rarely between the toes or fingers and on

the palms. They usually spread peripherally, burst, and leave scaly fringes (see Fig. 108). It may be so acute as to resemble a severe eczema and may lead to lymphangitis and enlargement of the inguinal glands, closely resembling a streptococcal infection. It is generally intensely pruritic.

FIG. 107.—Epidermophytosis
(Photograph kindly lent by Dr. R. Hallam)

Hyperkeratotic

In more chronic forms or phases there are indefinite scaly patches which, on the soles and more rarely on the palms, may be very hyperkeratotic and often fissured. The above forms can be combined or merge into each other. The nails are often involved, becoming discoloured, thickened and brittle, and raised from the nail-bed by scaly accumulation under the free border.

(3)—Diagnosis and Differential Diagnosis

Microscopical demonstration of fungus

Diagnosis depends on the demonstration of the fungus in the scales

FIG. 108.—Epidermophytosis. The lesions started as large vesicles. The other foot was symmetrically affected, and there was peeling between the toes. (Drs. A. D. McLachlan and W. H. Brown's case. From the Author's *Recent Advances in Dermatology*)

or the roofs of the vesicles (see Fig. 109; also Ringworm of the Smooth Skin, p. 459). Several specimens may have to be examined before

mycelium is found. In potassium hydroxide preparations from the hands and feet care must be taken not to mistake for true fungous

FIG. 109.—Photomicrograph showing mycelium of *Trichophyton interdigitale* embedded in skin-scale. (*American Journal of Public Health*, 1932)

mycelium an appearance which has been misleadingly named 'the mosaic fungus' but has recently been shown by Davidson and Gregory to consist of piles of the flat rhombic crystals of cholesterol. It differs

FIG. 110.—Scale from feet in 20 per cent potassium hydroxide, showing the so-called mosaic fungus. × 460. (*Journal of the American Medical Association*, 1935)

from true fungus in that its irregular broken-up branching 'threads' follow the outlines of the cells (see Fig. 110). The vesicular and superficial scaly varieties have to be distinguished from eczema. The hyperkeratotic *Differential* form may be confused with tertiary syphilis or with lichen verrucosus. *diagnosis*

(4)—Treatment

There is little tendency to spontaneous cure, although the symptoms may almost disappear in the winter. Acute bullous and vesicular eruptions should receive moist dressings of potassium permanganate 1 in 4,000 or monsol 1 in 500 of water. Free evaporation should be allowed and the feet rested. When the blistering has stopped and the erythema faded, calamine liniment with 1 per cent monsol can be used till the dry scaly stage is reached. Then Whitfield's ointment should be thoroughly rubbed in every morning and evening after washing with *Mycocten ointment* soap and water. An improved form of Whitfield's ointment is known as mycocten ointment. It is composed of lead oxide ointment (Danish Pharmacopoeia) 60, liquid paraffin, the ethyl ester of *para*-hydroxybenzoic acid, and salicylic acid of each 3 parts; its efficacy is increased by the addition of 5 per cent ammoniated mercury, which, however, is not always well tolerated. In obstinate cases it is well to alternate the *Fuchsin paint* ointment every fortnight with Castellani's fuchsin paint (see p. 458). This paint is especially useful for small crops of vesicles, which should be previously pricked and have their loose tags removed.

Legge and his co-workers obtained the best results with equal parts of glycerin and 7 per cent solution of iodine. Some otherwise intractable cases yield to 2 per cent cignolin, a synthetic chrysarobin substitute, in benzene. Thick horny masses must be removed by daily painting with salicylic acid 60 grains in 1 fluid ounce of alcohol 90 per cent, or by a barium sulphide depilatory. They also diminish under the influence of X-rays $\frac{1}{4}$ B to $\frac{1}{3}$ B (roughly 125 to 166 r) weekly, three or four times. The nails must not be neglected: they are a frequent source of reinfection, even though showing no clinical changes.

II.—MONILIAL INFECTIONS

1.—AETIOLOGY AND PATHOLOGY

Morphology 536.] Monilias are yeast-like fungi composed of budding oval spores. In culture they produce some mycelium but no asci. There are two chief varieties, *Monilia albicans* and *M. pinoyi*.

Habitat and pathogenicity Monilia can vegetate harmlessly on the human skin, from which it can be cultured in a large proportion of persons, especially from the toes, breasts, groins, and nails. Benham and Hopkins grew *M. albicans*, never from normal skin but, in 18 per cent of cases, from the tongue or faeces. If, therefore, *M. albicans* were found regularly in a given type of skin lesion there would be justification for considering it causal, and the source of infection might well be the alimentary tract. Cutaneous lesions are probably often due to inoculation by fingers contaminated from the stools. The pathogenicity of monilia is more facultative than

that of ringworm fungi. There is considerable experimental evidence
that monilia can be responsible for the conditions about to be described.
It flourishes best on a moist seborrhoeic type of skin and in situations
where there are naturally both warmth and moisture.

2.—CLINICAL PICTURE

The cutaneous lesions are almost as multiform as those of ringworm. *Lesions*
The sites of election are the perianal region in infants and the interdigital
spaces, groins, internatal cleft, submammary folds, axillae, and nail-

FIG. 111.—Moniliasis. The situation is unusual but the lesions themselves character-
istic. The scales were packed with spores and mycelium. (From the Author's
Recent Advances in Dermatology)

folds in adults. The lesions start as small red papulo-squamous patches
which become vesicular. The vesicles rupture to expose a bright red
smooth moist area, surrounded by a fringe of sodden opaque white
epithelium (see Fig. 111). The patches enlarge peripherally and heal in
the centre. Beyond the spreading edge are usually some isolated
vesicular outrunners. Moniliasis can, rarely, be so extensive and severe
as to lead to death.

The following are special clinical forms: *Special clini-*
                                                             cal forms

Thrush

In the mouths of babies, especially if bottle-fed, dry whitish patches
appear on the tongue or buccal mucosa. If scraped off they leave a raw
red surface. The white membrane contains masses of monilia, generally
M. pinoyi.

In the vagina monilial infection may cause a purulent vaginitis, especially in diabetics and pregnant women. It can also involve the anal canal, urethra, and glans penis.

Nursing infant type of eruption

Intestinal origin

This eruption is fairly common, either in perfectly normal infants or in those suffering from an associated gastro-intestinal involvement or from thrush in the mouth. The organisms probably always come from the intestine, where they may not have caused any symptoms. The lesions generally start in the perianal or inguino-crural region, whence the eruption spreads on to the buttocks, thighs, and abdomen and subsequently may involve the flexures of the elbows, folds of the neck, and elsewhere.

Interdigital lesions of feet and hands

When situated on the webs monilia often produces a denuded area, tapering towards the finger-tips, with the usual epithelial fringe; or the whole lesion may be sodden and leathery as in epidermophytosis, with a tendency to crack along the bottom of the fold. Monilia may also cause vesicular and scaly eczema of the palms, soles, fingers, and toes.
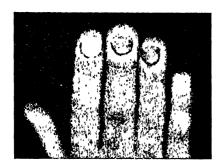
FIG. 112.—Monilial perionychia
(Photograph kindly lent by Dr. R. Hallam)

Perionychia

Those chiefly attacked are women who have their hands frequently in water or exposed to sugar. Manicuring contributes to its spread. The condition is sometimes associated with buccal or anal moniliasis. There is a bolster-like swelling of the nail-fold (see Fig. 112), which on being squeezed emits a bead of pus. The nail-plates, if attacked, assume the same appearance as is produced by ringworm fungi: their involvement is rarely primary.

Perlèche

The epithelium of the corners of the mouth becomes white, macerated, and wrinkled, and, in severe cases, cracked. Perlèche attacks children epidemically. There is also a sporadic form in women over the age of forty years whose resistance is lowered by some general illness. Salivation, often induced by dentures, is a predisposing factor.

Diabetic moniliasis

This form is commoner in women, attacking chiefly the genito-anal and submammary regions. The dermatophytosis may be the first indication of a metabolic disturbance, although their relationship is obscure.

Pustular moniliasis

This arises most frequently after prolonged application of wet com-

presses or immersion in baths. There are numerous superficial pustules with diffuse inflammation and maceration.

Furuncular type

Castellani described a monilial affection of the scalp, indistinguishable clinically from staphylococcal furunculosis.

3.–DIAGNOSIS

Diagnosis depends upon the repeated direct demonstration of copious monilia in the scales or roofs of vesicles. When these have been softened in potassium hydroxide solution and pressed into a thin smear, the organism can be recognized microscopically in a characteristic arrangement of mycelium and clusters of spores. Positive cultures, unless profuse and pure, are of small significance, since monilia can so frequently be grown from normal skin.

Demonstration of monilia

4.–TREATMENT

The patient must be carefully examined for metabolic disorders, especially diabetes mellitus.

After defaecation the perianal region should be bathed with a disinfectant and the hands thoroughly washed with antiseptic soap.

Internally, in severe systemic infections, potassium iodide should be given in large doses, even up to 15 grams thrice daily (Jacobson), or simple solution of iodine 5 to 15 minims or more thrice daily in milk. If these are not tolerated, Lugol's solution can be given intravenously, 0·6 to 1·0 c.c. in 10 c.c. of physiological saline.

Local treatment follows the same lines as for ringworm.

Thrush

The mouth should be cleaned with 2 per cent aqueous solution of borax and potassium chlorate and the membranes painted with 1 per cent gentian violet solution.

Perlèche

Monilial cases generally respond to a 6 to 10 per cent solution of silver nitrate, or 2 to 5 per cent gentian violet in 15 per cent alcohol, or 2 per cent iodine solution.

Perionychia

By means of a small camel-hair brush or orange-stick a small quantity of pure phenol or, better, undiluted neo-monsol should be introduced under the nail-fold once a day. Saturated solution of chrysarobin in chloroform is also useful.

5.—TINEA VERSICOLOR

(Synonym.—Pityriasis versicolor)

(1)—Aetiology

537.] Tinea versicolor is comparatively common in temperate zones. Similar, though not identical, affections are met with in the tropics. It is favoured by warmth and by profuse sweating. The cause is the proliferation in the horny layer of a fungus of the genus *Malassezia*, known as the *Microsporon furfur*. It is transmitted from one person to another directly or indirectly but is only mildly contagious. It is rare in childhood and old age and commoner in males than females.

(2)—Clinical Picture

Greenish-fawn well demarcated macules or sheets are seen on the upper part of the trunk and, more rarely, in the large flexures and elsewhere. The macules often start at the orifices of the lanugo hair-follicles. The skin may be slightly wrinkled but not obviously scaly. Nevertheless, very fine scales can be detached by light scratching. There is only exceptionally an inflammatory reaction.

Micro-scopical demonstration of fungus
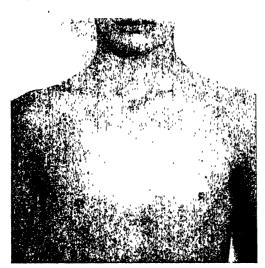
FIG. 113.—Tinea versicolor alba. Scales from white patches were full of fungus

(3)—Diagnosis and Differential Diagnosis

The diagnosis is very easily settled. Bits of the affected horny layer can be very readily scraped off. They should be placed in a drop of solution of potassium hydroxide and examined under high power without squashing them into a film. They are seen to be packed with copious clusters of round variable-sized spores and short mycelial threads.

Differential diagnosis Tinea versicolor may be mistaken for arsenical pigmentation, but the latter is more regular in pattern and affects the abdomen, hands, and feet more often than the upper part of the trunk. The oases of normal skin between the fawn patches may be taken for leucodermia, but the outlying islands in tinea versicolor should prevent this mistake. Occasionally it happens that the colour values are reversed, and in a person deeply pigmented by the sun, or in dark races, the fungus of tinea versicolor may cause loss of pigment (see Fig. 113).

(4)—Treatment

Although there is no tendency to spontaneous cure, the disease yields *Prognosis* rapidly to treatment but is apt to relapse if treatment is not persisted with for a week or two after apparent cure and if the underclothes are not disinfected by boiling.

After thorough washing with soap and water one of the following should be applied: (i) Whitfield's ointment; (ii) resorcinol and sulphur, 4 per cent of each in zinc paste; this may be increased in strength, if necessary, to secure mild exfoliation; (iii) sodium hypochlorite, 1 per cent solution, gently rubbed in twice daily, is more cleanly and may succeed.

6.–ERYTHRASMA

(1)—Aetiology

538.] The horny layer is invaded by *Microsporon minutissimum*, which, like *M. furfur*, belongs to the order of the Hyphomycetes. It is rather rare but widely distributed in Europe and in the tropics. It is very slightly contagious and chiefly attacks adult males.

(2)—Clinical Picture

A brownish well-defined patch with fine powdery scales grows very slowly on the upper part of the inner aspect of the thighs and sometimes in the axillae and occasionally in other intertriginous areas. The intensity at the edge is not greater than at the centre. There may be occasional irritation after sweating, or symptoms may be absent.

(3)—Diagnosis and Differential Diagnosis

The absolute diagnosis is made by finding *Microsporon minutissimum* *Microscopical* in the scales by the usual method; but the organism is so small that a *demonstration* $\frac{1}{12}$ inch oil-immersion lens is needed for its proper recognition as a mesh- *of fungus* work of extremely fine filaments and clusters of very small round spores.

Tinea cruris is distinguished by its more rapid development, inflamma- *Differential* tory reaction, clearing in the centre, and itching. Intertrigo is moist *diagnosis* and red, and its edge is ill-defined.

(4)—Treatment

Erythrasma is easily cured by the same measures as tinea versicolor.

III.—RARER INFECTIONS

1.–FAVUS

*(Synonym.—*Tinea favosa)

539.] This contagious disease, caused by fungi of the genus *Achorion*, *Aetiology* although rare in England, is not infrequently met with in Scotland and

Ireland, and is comparatively prevalent in Eastern Europe, Asia Minor, and the southern shores of the Mediterranean.

Clinical picture

It is characterized by sulphur-yellow cups (scutula), 2 or 3 mm. in diameter, embedded in the skin, each most commonly surrounding a hair (see Fig. 114). They consist of an agglomeration of fungus, leucocytes, and epithelial debris, and tend to coalesce into mortar-like masses. The involved hairs are seen microscopically to contain channels, which are mostly empty but here and there contain wavy filaments. A mousy odour may be noticed.

Differential diagnosis

Scutula occasionally form part of the eruption produced by *Microsporum quinckeanum* derived usually from mice but occasionally from horses. Generally, however, other types of lesion, such as red rings, herpetiform plaques, or kerion are present as well.

FIG. 114.—Favus. Two typical scutula
(Photograph kindly lent by
Dr. W. J. O'Donovan)

Prognosis

Favus can persist into adult life and causes permanent patchy cicatricial baldness. In addition to the scalp it may attack the nails or the glabrous skin, where it also leads to atrophy.

Treatment

Energetic treatment on the same lines as for ringworm is required.

2.–SPOROTRICHOSIS

(1)—Aetiology

540.] Sporotrichosis is due to one or several species of the genus *Sporothrix*, which occurs on plants and on most animals and therefore attacks especially gardeners and grooms. The average incubation period is nine days. Most cases have been reported from France and America, but instances have been noted in many other countries, including England. All ages and classes are susceptible. Susceptibility is increased by diabetes mellitus.

(2)—Clinical Picture

The lesions are subacute or chronic granulomas and may either be confined to the cutaneous and subcutaneous structures or involve the muscles, synovial membranes, periosteum, bones, mucous membranes, and occasionally the cerebrospinal system and viscera.

Primary cutaneous involvement

Cutaneous sporotrichosis is practically always primary. There are two chief clinical types: (i) at the site of a cutaneous trauma on an exposed portion of the body, generally the hand, a primary lesion develops,

resembling verrucous tuberculosis, while the lymphatics draining the infected area become inflamed, and along their course there appear, from time to time, hard nodules which may slowly turn into abscesses and ulcerate: (ii) multiple cutaneous and subcutaneous abscesses are distributed anywhere on the trunk and limbs. These, too, begin as hard nodules, which may even reach the size of a tangerine. From fistulous openings yellow viscid pus is discharged. Some of the abscesses break spontaneously in the centre to form a punched out or crateriform ulcer with indurated border.

(3)—Diagnosis

The diagnosis is best established by aspirating some exudate from *Culture* unbroken lesions and inoculating it on a glucose-agar medium. Some strains grow best at incubator temperature and some at room temperature. Growth appears between the fourth and tenth days. Microscopical examination of the culture reveals a mass of tangled branching fine septate mycelium. The small pear-shaped spores are arranged alongside the filaments, usually on short slight stems. Cultures from open lesions are less often successful and less conclusive. The parasites can very seldom be found in a direct smear preparation or stained section. If culture fails, support may be obtained from a positive agglutination *Agglutination* test. The intracutaneous test with sporotrichin, if negative, excludes *Skin test* sporotrichosis, but a positive reaction is not conclusive proof.

The disease may be mistaken for syphilitic gummata or tuberculous *Differential* nodules. *diagnosis*

(4)—Treatment

Though chronic, sporotrichosis can generally be cut short by appropriate measures. Potassium iodide should be given in ascending doses *Use of iodine* up to the limit of tolerance and should be continued for about six *compounds* weeks after the visible clinical signs have disappeared. If potassium iodide is not tolerated, a trial should be given to simple solution of iodine, Lugol's solution, sodium iodide, if necessary intravenously, or one of the organic iodine compounds. Occasionally tolerance can be increased by small doses of tincture of belladonna. Open lesions should be irrigated and dressed with Lugol's solution. The large unopened abscesses may be aspirated and similarly irrigated.

3.–TINEA IMBRICATA

(*Synonym.*—Tokelau ringworm)

(1)—Aetiology

541.] This is a strictly tropical disease, occurring mainly in India and *Geographical* the Far East and mostly attacking young male adults. It is caused by *distribution* the endodermophyton of Castellani, closely related to the trichophyta. In the scales the fungus is seen in enormous quantity in the form of septate mycelial threads with arthrospores but no conidia.

(2)—Clinical Picture

Progress of lesions   Small, round or oval, dark brown spots grow outwards and soon split in the centre, giving rise to a ring of large flaky scales attached at the periphery. While this ring expands, another brown spot appears in the centre and behaves as the first spot. This process is repeated until a number of concentric scaly rings develop. The scales partially cover each other like tiles on a roof. Sometimes the affection is more diffuse. It causes terribly severe itching, which prevents sleep and renders the victim unfit for work.

(3)—Treatment

Complete eradication is difficult. Castellani has found his fuchsin paint superior to other remedies. It must be applied once or twice daily to the same portion of the eruption for several weeks. When this has cleared, another portion is treated. Fairly good results are also obtained with the following paint: resorcinol 60 grains, acetic acid 60 minims, compound tincture of benzoin to 1 fluid ounce.

4.–PIEDRA

(*Synonyms.*—Trichosporosis nodosa; tinea nodosa)

(1)—Aetiology

Geographical distribution   542.] Piedra is found most frequently in South America, but a similar condition occasionally occurs in the British Isles and on the Continent of Europe. In Colombia it is ascribed to a kind of mucilaginous oil used *Microscopical appearances* by the natives for hair-dressing. According to Juhel-Renoy, if the hairs are soaked in solution of potassium hydroxide, the nodes can be seen to be composed of numerous spore-like bodies, twice the size of trichophyton spores, polyhedral in outline, forming a sort of tessellated mosaic, held together by a greenish soluble cement, in which are incorporated minute rods like bacteria.

(2)—Clinical Picture

Progress of lesions   The shafts of the hairs of the scalp, eye-lashes, moustache, or beard are dotted with grey, brown, or black, pin-point to pin-head sized, gritty nodes, which are either attached on one side of the shaft by an encircling sheath or may surround it. Eventually the nodes break up the cuticle and fray the cortex, so that the hair sometimes fractures.

(3)—Differential Diagnosis

Diagnosis from trichomycosis nodosa   Piedra should probably be distinguished from the commoner lepothrix (trichomycosis nodosa; trichomycosis palmellina), which most often affects the axillae and the pubes. In lepothrix the masses are apt to be less discrete and cover a greater surface of the hair and contain no indubitable fungus.

(4)—Treatment

Where practicable the hair should be shaved off and the skin dressed with Whitfield's ointment for a few days. Otherwise the hair should be cleaned with benzene and then with soap and water. Mercury biniodide 1 in 2,000 of 50 per cent alcohol must then be dabbed on daily for several weeks.

5.–LEPOTHRIX

(*Synonyms.*—Trichomycosis nodosa; trichomycosis palmellina)

(1)—Aetiology

543.] Lepothrix occurs fairly commonly in all grades of society, is favoured by heat and moisture, and is thought to be parasitic. The *Microscopical* nodular masses appear to be made up of micro-organisms, chiefly cocci, *appearances* held together by a homogeneous substance. Castellani found a bacillus-like fungus, alone in the yellow variety and associated with cocci in the black and red varieties. In some red varieties *Chromobacterium prodigiosum* has been noted; but the organisms found are not constant and may be few in number, the masses consisting chiefly of transparent chitinous material.

(2)—Clinical Picture

On the shafts of the hairs of the axillae and pubes are seen various amounts and kinds of accretions. These may form either distinct nodes or irregular masses partially or entirely surrounding a large part of the shaft. Reddish brown, yellow, red, and black varieties have been described. The sweat is sometimes tinted red.

The accretions may be soft and easily removable or hard and firmly adherent. They can bring about brush-like fractures of the hairs. Castellani described yellow, black, and red varieties (trichomycosis flava, nigra, and rubra) of the axillae in Ceylon, which he considered distinct from the forms met with in temperate zones.

(3)—Treatment

Crocker advised shaving and the application of mercuric chloride 1 in 2,000. Castellani (1934) recommended dabbing with formalin solution 4 in 180 of alcohol several times daily and applying at night a 2 to 5 per cent sulphur ointment.

IV.—DERMATOPHYTIDES

1.–DEFINITION

544.] Some exanthematic or distant eruptions are met with, which may be supposed to be due to haematogenous dissemination of fungus from a primary focus, together with an allergic supersensitiveness of the skin.

2.—AETIOLOGY AND CLINICAL PICTURE

Clinical types

The commonest exanthematic dermatophytide is the lichenoid, a symmetrical eruption of groups of minute pink conical follicular papules (see Fig. 115). It may also resemble lichen planus or spinulosus. In an early stage it is sometimes scarlatiniform and followed by desquamation of the palms. Other forms include maculo-papules, urticaria, erythema nodosum, and erythema multiforme.

Associated organisms

Dermatophytides of this kind are commonest in infections, often from an animal, with virulent fungus, especially *Trichophyton ectothrix gypseum*, causing a hypertrophic granulomatous lesion. The above individual clinical forms are not, however, strictly related to any particular group of fungi and can result even from superficial ringworm, especially after irritating local applications.

Allergic factor

The supersensitive state of the skin is shown by intracutaneous tests with fungal extracts, such as trichophytin; but, as there is no standard preparation, the results of comparative tests with it must be interpreted with great caution.

Eczema-tous form

Recently there has been accumulating evidence that dermatophytides may take the form of eczema; in particular, 'dyshidrotic eczema of the hands' (pompholyx) is thought to be in a large proportion of cases an epidermophytide from the feet.

FIG. 115.—Lichenoid dermatophytide
(Photograph kindly lent by Dr. J. T. Ingram)

Often fungus cannot be demonstrated in the hands, but the eczema disappears if the feet are adequately treated.

Levurides

Till recently monilia had been held responsible only for the typical localized clinical pictures described under moniliasis, which should only be accepted as such if large quantities of the organism can be demonstrated in situ. But, recently, distant secondary eruptions, analogous to other dermatophytides, have been ascribed to it and called levurides. They take the form either of eczema or of eczematoid erythemato-squamous eruptions, such as are so frequently called seborrhoeic dermatitis. In these eruptions, which disappear and reappear with the primary lesion, monilia can either not be found or only be demonstrated by culture.

3.–TREATMENT

The main task is to eradicate the primary focus, and this is sometimes all that is required. In view, however, of the fact that the primary focus is often very difficult to eradicate, some attempt may be made to diminish the sensitiveness of the skin to the fungus or its products. Some success has been achieved by giving intracutaneous injections of gradually increasing doses of trichophytin (in ringworm infections) or levurin or oidiomycin (in monilial infections), or by clasovaccines (Jausion and Sohier). Of the latter the initial dose is 0·5 c.c. and the maximum 3 c.c. subcutaneously. Generally only six injections are found necessary, given at an average interval of five days.

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FUNGUS FOOT

See MYCETOMA

FURUNCULOSIS

See BOILS AND CARBUNCLES, Vol. II, p. 547

GALL-BLADDER AND BILE-DUCTS

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Reference may also be made to the following titles:

ABDOMINAL PAIN AND   FOETUS DISEASES
    ACUTE ABDOMINAL   INTESTINAL OBSTRUCTION
    EMERGENCIES   JAUNDICE
            LIVER DISEASES

1.–ANATOMY

(1)—Gall-Bladder

545.] There are certain points in the anatomy of the biliary passages which it is important to bear in mind as they furnish the key to some of the problems in the pathology and clinical symptoms of biliary disease. The gall-bladder is a pear-shaped sac, lined by columnar epithelium thrown into folds. It has a thin submucous coat—an open meshwork of delicate fibrous tissue—separating the mucosa from the muscular coat. The latter is made up of interlacing muscular bundles and elastic fibres, the muscular fibres being present in greatest abundance at the neck of the gall-bladder. The muscular coat is continued along the cystic duct where the fibres extend into the spiral fold—the valves of Heister. Towards the common bile-duct the muscle-fibres become more scanty, and the wall of the cystic duct contains more fibrous tissue.

Blood supply   The subperitoneal coat of the gall-bladder is a well-defined layer of cellular fibrous tissue, and in it run most of the blood and lymphatic vessels and the nerves of the organ. The cystic artery, arising as a rule from the right hepatic artery, is a large vessel relative to the size of the organ it supplies. Its origin and course are subject to great variation—an important point in the surgery of the gall-bladder. The artery may cross in front of or behind the common bile-duct, may be duplicated, and may lie along the cystic duct, or at some distance from it. The veins of the gall-bladder run, for the most part, directly into the liver and do not accompany the artery.

Lymph supply   There is a very rich lymphatic drainage system in the wall of the gall-bladder. The lymphatics converge on the cystic lymphatic gland which lies closely applied to the cystic artery. This gland is always enlarged in infections of the gall-bladder; hence the name 'sentinel gland'. Some lymphatic vessels pass directly into the liver across the bare area of the gall-bladder wall, and their presence explains the localized hepatitis so constantly found in that part of the liver contiguous to the gall-bladder when the latter is inflamed.

Nervous connexions   The gall-bladder is richly supplied with both sympathetic and parasympathetic nerves (see Fig. 116); the sympathetic nerves, with cell stations along the cystic duct, are connected with the hepatic plexus

and, through the coeliac ganglion and splanchnic nerves. with the lower
six thoracic segments of the cord. but particularly with the ninth thoracic
segment; hence the radiating intercostal pain and the tenderness over
the somatic distribution of the ninth intercostal nerve. so common in
biliary disease. The connexion between the hepatic and phrenic plexuses
of the sympathetic, and on through the sensory fibres of the phrenic
nerve, gives the anatomical explanation of the shoulder-tip pain found
in some cases of biliary
disease without any ob-
vious subphrenic inflam-
mation.

(2)—Bile-Ducts

The structure of the bile-
ducts differs from that of
the gall-bladder in several
respects. In the first place
the muscular coat of the
ducts is poorly developed
and, in parts, defective,
and its place is taken by
fibrous tissue. In the wall
of the duct there are long,
coiled, tubular glands
which secrete a watery
fluid. At the lower end
of the common bile-duct
there is an aggregation of
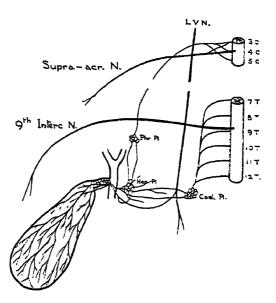
FIG. 116.—Nerve connexions of gall-bladder
through hepatic plexus of sympathetic and vagus

interlacing oblique and circular muscle fibres—the sphincter of Oddi.
This muscular sphincter interlaces with the muscular coat of the duo-
denum and may enclose the termination of the duct of Wirsung from
the pancreas as well as the bile-duct. There is a rich lymph drainage
system from both extra- and intra-hepatic bile-ducts; hence the pro-
nounced symptoms of septic absorption which tend to accompany
recurring obstruction of an infected common bile-duct.

2.–PHYSIOLOGY

546.] The function of the gall-bladder is to store and concentrate the *Function of*
bile pending the intermittent requirements of digestion. The gall- *gall-bladder*
bladder can concentrate the bile tenfold within 24 hours; thus its
limited capacity (50 c.c.) is adequate for bile storage between meals.
From its lining membrane mucus is added to the bile and this secretion
becomes a dominant factor when the gall-bladder is inflamed. From the
glands embedded in the wall of the common bile-duct a watery secre-
tion is poured out and dilutes the bile. In complete obstruction of the

Formation of 'white bile' common duct, when the pressure within the duct rises to a point at which the liver can no longer secrete bile, the glands in the duct wall continue to give off their watery secretion. Thus gradually, through lymph absorption, bile is removed and is replaced by a clear colourless secretion which contains none of the usual chemical constituents of bile—the so-called 'white bile' of prolonged biliary obstruction. This replacement of dark by white bile occurs much earlier if the gall-bladder, as a result of old inflammatory changes, is incapable of carrying on its concentrating function.

3.–GALL-STONES

Incidence 547.] The frequency of calculus formation within the gall-bladder has been variously estimated as from 5 to 10 per cent of all adult subjects. It is undoubtedly commoner in the female sex (5 females to 1 male) and especially in stout multiparae. Whereas evidence of infection of the gall-bladder wall frequently accompanies the presence of gall-stones, the latter may be found in an organ which shows no trace of bacterial invasion. Metabolic disturbances would appear to be the underlying cause of the formation of certain types of calculi.

(1)—Metabolic Gall-Stones

Cholesterol stone The cholesterol stone, a single ovoid stone composed almost entirely of radiate interlacing cholesterol crystals, is not infrequently found in a gall-bladder to all appearance normal. An excess of cholesterol in the bile, or a relative inadequacy of the bile-salts which maintain cholesterol in colloidal suspension, is the probable explanation of concretion formation round an organic nucleus.

(a) Impaction with Mucocele Formation

A 'cholesterol solitaire' may lie in the gall-bladder for a long time without giving rise to any symptoms. Should it chance to find its way into the neck of the gall-bladder and block the entrance of the cystic duct, an attack of afebrile biliary colic results.

Clinical picture of single cholesterol stone A very typical clinical picture is the onset, in the midst of good health, of a severe attack of colic, coming on often as the patient goes to bed, lasting for a few hours, then passing and leaving the patient with no ill-effects except the memory of an agonizing pain. Months of good health and undisturbed digestion may elapse before a second bout of colic supervenes. Such attacks may continue to occur at irregular intervals over a period of years, but complications are apt to appear. Thus one attack may fail to resolve as did its forerunners. The patient is left with a persistent discomfort below the right costal margin. Flatulence, epigastric fullness, and subcostal ache follow regularly after meals, especially if fatty foods be taken. A soreness in the right scapular region, often attributed to rheumatism, becomes habitual, and stooping brings on uneasiness and even pain.

Abdominal examination at this stage may reveal a painless pyriform

swelling below the right costal margin, easily recognizable as a dis- *Mucocele of*
tended gall-bladder. A radiological examination after iodopnthalein *gall-bladder*
has been given shows no gall-bladder shadow, and, if operation is
performed, there is found a large gall-bladder distended with mucus
and with a single ovoid stone impacted in the neck—a mucocele of the
gall-bladder.

(b) Acute Obstructive Cholecystitis

More frequently prolonged impaction of a stone is accompanied by *Obstruction*
infection of the obstructed gall-bladder. The initial pain is followed by a *with infection*
mild rigor, with a rise of temperature
and of pulse-rate. A constant ache
and a sensation of upper abdominal
tightness develop, and a catch in the
breathing indicates subdiaphragmatic
peritoneal irritation.

On examination the patient is
flushed and shows distress: the
tongue is coated, the upper right
quadrant of the abdomen is rigid and
resistant, and palpation elicits pro-
nounced tenderness and a protective
guarding by the abdominal muscu-
lature. The patient may show a faint
tinge of jaundice and a trace of bile
in the urine, for a hepatitis accom-
panies the obstructive cholecystitis.
Examination of the chest discloses a
slight dullness on percussion at the
base of the right lung, and some
crepitations can be heard on inspira-
tion—the rigid right cupola of the
diaphragm having led to some hypo-
static congestion of the lower lobe
of the right lung (see Fig. 117). After
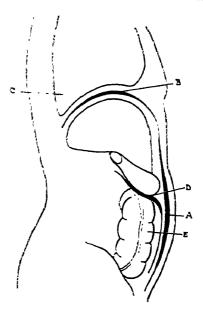
FIG. 117.—Acute obstructive chole-
cystitis. A, boarded abdominal
muscles. B, boarded diaphragm.
C, oedema at base of right lung.
D, adherent omentum. E, dis-
tended colon

36 to 48 hours a prominent feature in the case may be flatulent disten-
sion of the right side of the abdomen, and the caecum may be seen to
stand out prominently, so much so that it is tempting to think of an
organic obstruction of the colon. This distension is explained by the
oedema of the hepatic flexure of the colon in apposition with the
inflamed gall-bladder.

Although the diagnosis of acute obstructive cholecystitis is, as a rule, *Factors*
easy, its treatment requires judgement and watchful care. As a rule the *determining*
infection is mixed and due to *B. coli* and streptococcus, the gall-bladder *treatment*
becomes tensely distended with a mixture of bile and muco-pus, and
the inflammation reaches its acme in about 48 hours, then tending to
subside. At this point the secretion of mucus lessens and the absorptive

function of the wall reasserts itself with a consequent reduction of tension, permitting the impacted stone to recede. It is customary, therefore, in middle-aged subjects with resilient gall-bladder walls, no vascular degeneration and but mild or moderately virulent infection, for the organ to withstand the combined effects of tension and infection and to weather the acute attack under expectant treatment. In some cases, however, when the infection is partly anaerobic (*Clostridium welchii*) and especially in elderly subjects, in whom, owing to vascular rigidity, tension more readily compromises the vitality of the wall, necrosis, first of the mucous membrane and then of the whole thickness of the wall, leads to leakage and formation of subhepatic or subphrenic abscess.

Operation for acute obstructive cholecystitis

It is necessary, therefore, to be watchful at the end of 48 hours, when in the ordinary course of events symptoms should show a tendency to relent and to subside, for signs of increasing toxaemia as evidenced by continued distress, repeated vomiting, dry tongue, rising pulse-rate, and increasing tenderness. Should these unfavourable features develop, immediate operation under local anaesthesia, supplemented by gas and oxygen, should be undertaken, the minimum being done which will relieve symptoms and arrest danger to life. This consists in opening the gall-bladder, evacuating the muco-purulent contents, and dislodging and removing the impacted stone. No attempt should be made to remove the gall-bladder unless it is gangrenous, when all devitalized portions may be clipped away.

Indications and contra-indications for operation

The policy of operating on all cases of acute obstructive cholecystitis whenever diagnosed, although strongly advocated by many American surgeons, should be deprecated; cholecystectomy in such circumstances is often difficult and fraught with risk, and a drainage operation is but palliative. When possible, as it is in more than 80 per cent of cases, operation should be postponed until the acute phase is over, when the accompanying hepatitis has subsided and removal of the diseased and crippled gall-bladder may be deliberately and safely undertaken. An interval of ten days to a fortnight should be allowed to elapse.

Cholecyst-ectomy

Operation in this subacute phase should consist of cholecystectomy. After separation of the adherent omentum the thickened and distended gall-bladder should be tapped with a large trocar and cannula. This gives a freer exposure of its neck, round which there is often considerable oedema, rendering identification of the common bile-duct difficult. In order to ensure that no damage is done to the duct or hepatic vessels, it is often advisable to dissect back a cuff from the neck of the gall-bladder after incision down to its submucous coat and to ligate the cystic duct within this cuff. By this submucous approach to the cystic duct a shield of tissue protects the important structures which are concealed by oedema.

(2)—Pigment Gall-Stones

Characters and effects

These are found most typically in acholuric jaundice. Usually small and multiple they are black, irregularly spiculated, and cinder-like in

appearance. They form in a healthy gall-bladder as a result of deposition from heavily pigment-laden bile. Passing down the ducts they may give rise to biliary colic, but more frequently they cause no symptoms and are found at operation or necropsy in a large proportion of cases of haemolytic ictero-anaemia. Apart from this disease, however, minute pigment granules may form the nuclei of multiple cholesterol stones when some metabolic variation leads to a subsequent excess of cholesterol in the bile, and in the opinion of some observers, notably Rovsing, minute pigment granules, forming in the smaller bile-ducts and carried to the gall-bladder, are the most fertile source of stone formation in this organ.

(3)—Cholesterosis of Gall-Bladder

This condition, sometimes known as the 'strawberry gall-bladder', in *Clinical* which deposits of lipoid material are present in the mucosal lining of the *importance* gall-bladder (see Fig. 118), has a clinical importance for two reasons. First, it is sometimes the forerunner of cholesterol stones, and secondly, even without stone formation, it may give rise to symptoms resembling biliary colic, which disappear after extirpation of the lipoid-laden gall-bladder. The aetiology of the condition is *Aetiology* still obscure. It usually occurs in association *and morbid* with a very mild and chronic indolent in-*anatomy* fection of the gall-bladder wall, but has been found in gall-bladders without any microscopic evidence of present or ante-cedent inflammation. The cells covering the villi of the mucosa are swollen and laden with cholesterol ester, which gives a yellow-ish white freckled appearance to the mucous membrane. In places small lipoid-laden papillomas are seen, and the detachment of these may furnish the nuclei for mulberry-like cholesterol stones. This condition is
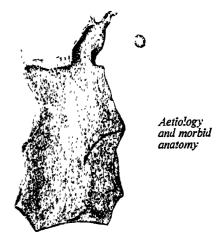
FIG. 118.—Cholesterosis of the gall-bladder. Villi laden with lipoid material. Con-dition stopping abruptly at neck of organ. One small cholesterol stone in gall-bladder

sometimes found in patients in whom an erroneous diagnosis of gall-stones has been made. At operation minute opaque yellowish spots may be descried through the slightly thickened gall-bladder wall. In such circumstances removal of the organ is indicated, as there is now *Treatment* sufficient evidence that cholecystectomy will in all probability relieve the patient of symptoms. It is doubtful if it is yet ever possible to make *Problem of* a pre-operative diagnosis of the condition, as it does not give any *pre-operative* *diagnosis* characteristic radiological picture, and the presence of an excess of cholesterol in the bile is unreliable evidence of its presence.

4.–CHOLECYSTITIS

548.] Judging by post-mortem findings infection of the gall-bladder is common. In its acute form it is seldom encountered apart from obstruction of the gall-bladder neck or cystic duct, usually by a gall-stone. Mild degrees of acute infection doubtless occur in the absence of obstruction, but they have rarely been displayed either on the operation table or at necropsy. In tropical countries acute cholecystitis without stone is met with. Infection of the gall-bladder is more prone to be of a very subacute or chronic type, and of the various portals of infection that by the blood-stream would seem to be the most frequent. Various micro-organisms have been isolated, both from the bile and the gall-bladder wall, in such cases. In order of frequency these are streptococci, *B. coli*, staphylococci, *B. typhosum*, and *Cl. welchii*, the first two mentioned accounting for 80 per cent of all cases. Frequently when the bile is sterile a growth of streptococci or *B. coli* may be obtained from the gall-bladder wall or the cystic lymphatic gland.

Bacteriology

The clinical importance of gall-bladder infection is twofold: (i) by interfering with the normal filling and emptying of the gall-bladder, i.e. producing stasis, it predisposes to the formation of gall-stones, and (ii) by harbouring a chronic indolent infection in its wall the gall-bladder may act as a focus of infection, from which toxic products are absorbed and repeated infection may be carried to other tissues.

Results of gall-bladder infection

(1)—Post-Infection Gall-Stones

Characters
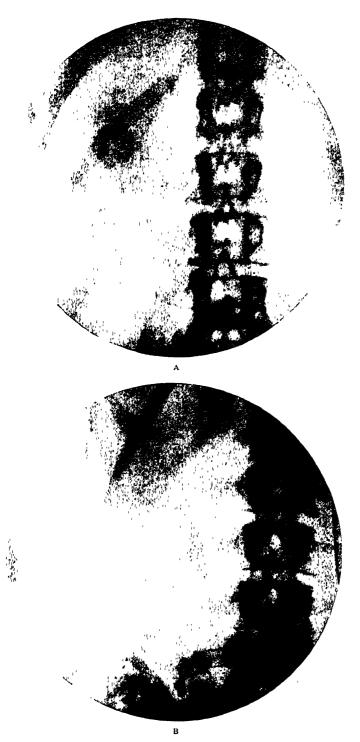
The stones forming in an already infected gall-bladder are usually many in number and mixed in structure. They have a soft pigmented centre, composed of organic material and a mixture of cholesterol and calcium bilirubin and often demonstrable micro-organisms, and a harder shell which may be laminated and contain a preponderance of calcium bilirubin, along with a lesser amount of cholesterol. Thus they may be visible as ring-like shadows in an X-ray picture (see Plate VI). Frequently there are many stones of the same size and structure, faceted and obviously of the same origin and age. Not infrequently, among a large number of such stones, one large ovoid stone may be found. The latter has a shell of cholesterol and calcium bilirubin enclosing a typical radiate cholesterol stone. Aschoff termed this a 'combination stone', and it almost certainly represents a primary aseptic formation which preceded the gall-bladder infection with its brood of septic stones.

'Combination stone'

(2)—Symptomatology of Chronic Cholecystitis

The clinical picture of chronic gall-bladder infection depends partly on mechanical difficulties caused by the presence of stones or inflammatory swelling of the cystic duct, and partly on the effects of toxic absorption from the diseased organ. The outstanding complaint is of a chronic flatulent dyspepsia. The flatulence comes on immediately after

Flatulence

A

B

Radiographs of gall-bladder after iodophthalein. A. Shows non-functioning gall-bladder containing opaque gall-stones: three stones in cystic duct and three in common bile-duct. B. Taken eighteen hours after dye and two hours after fatty meal, shows contracted gall-bladder containing dye and six negative shadows—cholesterol stones

PLATE VI

eating, is worse when greasy and fatty foods have been taken. and a
heavy meal does not give. as in the case of duodenal ulcer. a temporary
relief but is almost immediately regretted.

Associated with the flatulence there may be a dull aching pain below *Pain*
the right costal margin or at the angle of the right scapula. Stooping
may bring on or aggravate the pain, as may active exercise. Exposure
to cold is apt to light up an acute subcostal discomfort. which may have
been dormant for some time. Occasionally short and sharp attacks of
severe pain, extending from the epigastrium round the lower ribs on
both sides, indicate that a stone has become impacted in the cystic duct,
or has passed down the common duct. Owing to the flatulence and to
the aching after exercise, the patient tends to restrict her activities and
to put on weight, and the laying on of fat further increases the breathless-
ness and the disinclination for active exercise.

Heartburn is quite common in cholecystitis. in spite of the fact that *Heartburn*
in quite 50 per cent of cases hypochlorhydria is present. Jaundice is only *Jaundice*
found either in a slight and transient form after an acute exacerbation
of cholecystitis, or in a more pronounced degree when a stone has
lodged in the common bile-duct.

In some patients local symptoms and signs are comparatively slight,
and leading complaints are of nausea. headaches. and rheumatic pains.
especially in the muscles of the neck and back, and occasionally in
joints. These symptoms all betoken a chronic toxaemia. the cause of
which may at first seem obscure.

Similarly cardiac symptoms in the form of praecordial pain and a sense *Cardiac*
of constriction, palpitation. and breathlessness may dominate the picture *symptoms*
and overshadow the milder digestive complaints. It is only after close
questioning and careful physical examination that the primary morbid
change in the gall-bladder becomes evident and that organ suspect.
The proof that the general 'rheumatic' and cardiac symptoms depend
on the gall-bladder infection is difficult to establish in the individual
case except by operative extirpation of the gall-bladder. In a long series
of post-operative cases, examined in a systematic follow-up, the most
striking improvements recorded by the patients were in the disappear-
ance of former rheumatic pains and, in a certain number, of the prae-
cordial constriction, anginal pains, and palpitations, which had followed
mild physical exertion.

An exact diagnosis of chronic cholecystitis, with or without stones. *Diagnosis*
is facilitated by employing the two supplementary clinical methods
which are now available, namely, duodenal intubation, and X-ray
examination following the administration of a dye—cholecystography.
The recovery of bile from the duodenum, after the passage of the duo- *Duodenal*
denal tube and the administration of magnesium sulphate, may give *tube in diagnosis*
conclusive evidence, e.g. when the bile contains biliary sand, pus cells,
and numerous micro-organisms. A negative finding. however, is of
much less value, for a specimen of apparently normal bile may be
obtained in a case in which there is a well-marked intramural infection

of the gall-bladder and even when stones are present. The distinction between duct, gall-bladder, and liver bile, as described in the Meltzer-Lyon test, is not sufficiently easily obtained, even in normal individuals, to make this method of examination reliable for the diagnosis of the finer gradations of disease. It is when the common bile-duct is infected that the test is especially valuable, not only in diagnosis but in assessing the effects of medical treatment.

X-ray diagnosis

Straight X-ray films, that is exposure made without the use of a dye, will often show the presence of gall-stones, the shadows being of several types. Perhaps the commonest is the signet-ring variety in which a cholesterol core is encased in a covering containing calcium bilirubin. Sometimes, however, stones containing a considerable quantity of calcium bicarbonate may give a uniformly dense shadow. These are usually found in a gall-bladder the cystic duct of which has been blocked for some time. In some cases large barrel-shaped stones, showing irregular deposits of calcium, are clearly visible. A deposit of biliary mud or sand containing calcium may cast a shadow outlining the fundus of the gall-bladder. The majority of gall-stones, consisting mainly of cholesterol, do not give a shadow in the ordinary X-ray film. It is the exception for stones in the common bile-duct to be shown by X-rays.

(3)—Cholecystography

Administration of dye

Since Graham introduced the method of visualizing the gall-bladder in an X-ray picture by giving the dye sodium tetraiodophenolphthalein (iodophthalein), which is excreted by the liver and concentrated along with the bile in the gall-bladder, a much greater degree of accuracy in diagnosis has been possible. Originally intravenous administration was practised, but now the dye is usually given by the mouth with almost equally reliable results. The dose by the mouth is 0·04 to 0·06 gram per kilogram of body-weight, up to a total of 5 grams ($\frac{1}{3}$ to $\frac{1}{2}$ grain per pound of body-weight, up to 75 grains). Not more than 3 grams (45 grains) should be given intravenously.

Briefly the significant findings are:

Significant findings

(i) Absence of the gall-bladder shadow is most significant, as it usually means that the cystic duct is blocked and that the gall-bladder is pathological.

(ii) The gall-bladder is outlined and contains negative shadows. These indicate cholesterol stones displacing the dye-laden bile. Care must be taken to exclude the negative shadows cast by gas in an overlying portion of bowel (see Plate VI).

(iii) The gall-bladder shadow is faint and irregular in outline or may show a filling defect, indicating a papillomatous growth. It is in the depth of the shadow and the significance to be attached to faint shadows that the main difficulties of interpretation arise.

It is well to supplement cholecystography with a barium meal examination of the stomach and duodenum in all doubtful cases, as, in the stout female, duodenal ulcer and cholecystitis mimic each other closely.

(4)—The Cholecysto-Duodenal Syndrome

The frequency of biliary disease in the stout middle-aged housewife suggests this diagnosis when such a patient complains of flatulence, epigastric fullness, and heartburn after food, and occasional spasms of upper abdominal pain. First of all by operative exposure, and latterly by radiological findings, it has been found that many of these patients have normal gall-bladders but are suffering from duodenal ulcer. They never complain of hunger pains, as they habitually eat between meals and allay the pain ere it is recognizable. The frequent eating, usually of carbohydrate, leads to obesity and causes gastric flatulence. The severe attacks of pain, often mistaken for mild biliary colic, are difficult to explain but are probably due to pylorospasm.

Cholecystography shows a normal gall-bladder shadow, and screening after a barium meal a marked deformity of the duodenal cap.

X-ray picture

(5)—Coincident Infections

In both the diagnosis and treatment of biliary disease it must be borne in mind that coincident lesions are not infrequent in the
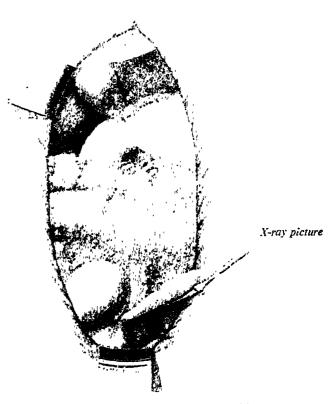
FIG. 119.—Abdominal triad. Cholecystitis with gall-stones, duodenal ulcer, and subacute appendicitis

vermiform appendix and in the duodenum (see Fig. 119). The clinical *Problems in* picture and the differential diagnosis are disconcerting and difficult if the *diagnosis* possibility of this triad of lesions is not considered. At one period one lesion may assert itself, at another time another, and in some cases, particularly in highly strung subjects, the variation in complaint may suggest a large functional element in the case. I have had to deal surgically with 40 patients in whom a chronic lesion was found in the appendix, gall-bladder, and duodenum, and all three lesions were dealt with. In a number of cases in which one or other of the lesions was overlooked at operation subsequent operative measures have been required. In several of these cases a similar streptococcus has been isolated at

operation from the gall-bladder, the duodenal ulcer, and the inflamed appendix.

(6)—Prognosis

It is unquestionable that patients may live for years in tolerably good health with a chronic inflammation in the wall of the gall-bladder provided they take care to avoid heavy and fatty foods and large meals. When gall-stones are present symptoms may remain in abeyance for years at a time. Sooner or later, however, some complication is liable to supervene. This may be obstructive cholecystitis, the lodgment of a stone in the common duct, a sudden acute pancreatitis, the development of chronic toxic manifestations, or the onset of malignant disease of the gall-bladder. The liability to these complications makes it desirable in younger subjects to institute active surgical treatment, whereas in older patients palliative measures may be deemed advisable.

The surgical treatment now recommended is the extirpation of the gall-bladder along with any stone within it. Cholecystectomy has, in practised hands, a mortality of 2 per cent. The outlook is extremely good provided no stone has been left behind in the common bile-duct. Recurrence of symptoms should suggest that some other unrecognized lesion in the stomach, duodenum, pancreas, or common bile-duct was present and was not dealt with.

(7)—Post-Operative Treatment

After cholecystectomy the patient should, for a number of months, live on a diet from which cooked fats are largely eliminated, otherwise a varied diet may be allowed. A saline aperient should be taken every morning and physical exercise, including games, should be encouraged after the first six months.

5.–CARCINOMA OF GALL-BLADDER

Incidence

549.] Malignant disease of the gall-bladder is not uncommon. In 1,100 operations on the biliary passages I have met with it in forty cases. In over 90 per cent of these there had been antecedent cholecystitis with gall-stones; it may thus be regarded as a late complication of cholelithiasis. The disease may start in any part of the gall-bladder—fundus, body, or infundibulum—and may be either a soft polypoidal growth or, more commonly, a hard infiltrating scirrhous carcinoma (see Fig. 120). It spreads by way of the lymphatics and at a comparatively early stage involves the adjacent liver by direct extension, the cystic lymphatic gland and thence the glands along the common duct and those in the portal fissure. When the disease begins in the neck of the gall-bladder it may occlude the lumen of the cystic duct and cause a mucocele of the

Diagnosis of malignant gall-bladder

organ. The patient, who gives a previous history suggesting gall-stones, then complains of a constant aching pain under the right costal margin,

and the distended gall-bladder may be palpable. More commonly the disease is not suspected until the patient shows progressive jaundice. This is due to pressure of invaded lymphatic glands on the common bile-duct, by which time the disease has progressed beyond the hope of radical surgical treatment.

The difficulty of early diagnosis and the lines of spread of the disease combine to make the prognosis almost uniformly bad. The only cases in which successful extirpation of the disease has been possible are those in which it was found accidentally at operation for gall-stones, and then the presence of carcinoma was revealed by histological examination of the thickened gall-bladder wall. Treatment, therefore, must be mainly prophylactic, and indeed the chance of subsequent malignancy is one of the strongest arguments for removing the diseased gall-bladder when operating for gall-stones.

Prophylaxis

Even when the gall-bladder with its contained malignant disease has been removed, and the lymphatic glands and liver have apparently not been involved, the prognosis is by no means good. Carcinoma of the gall-bladder and bile-ducts must therefore be considered a very serious disease, difficult to diagnose at a stage when extirpation is possible, and liable to early recurrence after an apparently successful operation. When recurrence takes place treatment by radiotherapy may be tried but with only faint hope of success. The disease in the first place is not very radiosensitive, and in the second place effective therapy is hampered by the proximity of liver, pancreas, and adrenals.

Prognosis
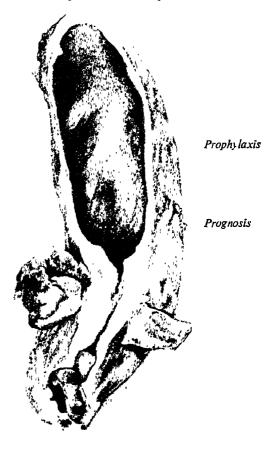
Fig. 120.—Carcinoma of gall-bladder associated with multiple gall-stones

6.–DISEASES OF BILE-DUCTS

(1)—Stone in Common Bile-Duct

550.] One of the serious complications of gall-stones is the lodging of a stone in the common duct. Smaller stones from the gall-bladder may, and frequently do, pass down and successfully negotiate the common duct and the papilla.

(a) Intermittent Obstruction

If, however, a stone fails to pass on into the duodenum it leads to intermittent obstruction of the duct, which dilates and becomes infected, and we get the syndrome of cholangitis and intermittent obstruction. Owing to the stasis and infection a soft deposit of 'biliary mud' takes place, coating the stone and often silting up the duct. The typical syndrome, so graphically described by Charcot and known as 'intermittent biliary fever of Charcot', consisting of intermittent attacks of pain, often accompanied by a rigor and fever, followed by jaundice,

'Charcot syndrome'

FIG. 121.—Consecutive suppurative hepatitis. Gall-stone impacted in ampulla of Vater. Infective cholangitis leading to multiple abscesses in liver

with bile-laden urine and pale stools, associated with loss of weight and deterioration of general health, is pathognomonic of the condition, which, if left untreated, may result in suppurative cholangitis and multiple liver abscesses (see Fig. 121). Not infrequently, however, some of the classical symptoms may be absent. Thus the patient may deny ever having had any severe pain, jaundice may have been so slight as almost to escape notice, and rigors may not have occurred.

Atypical clinical pictures

In my experience such atypical clinical pictures are usually met with when a large number of stones from the gall-bladder have passed through a dilated cystic duct and lodged in the common duct. The bile percolates between the stones as water through a gravel bed, colic and jaundice are never outstanding features, and an obscure relapsing febrile illness, with an occasional icteric tinge of the skin, suggests the

possibility of infected biliary passages, partly choked with 'biliary mud' and stones. In these cases progressive loss of weight and deterioration of general health are marked features.

(b) Complete Obstruction

Another picture is that, following a more or less severe attack of epigastric pain, with or without fever, the patient becomes progressively more and more jaundiced, the stools clay coloured, and the urine rich in bile. This suggests that a single stone in the duct has become impacted in the ampulla of Vater and completely blocked the passage. An antecedent history of biliary trouble can usually be obtained in such a case. When a stone in the common duct is suspected, and especially if jaundice is present, it is unwise to attempt cholecystography. Bile laden with dye, if it should chance to enter the pancreatic duct, may produce a fulminating pancreatitis as shown experimentally by Bruce Dick. Stones in the common duct seldom show in a straight X-ray picture. Diagnosis is, however, seldom in doubt, and, when it is made, surgical treatment should not be delayed longer than to allow an acute exacerbation to subside. When jaundice shows no sign of waning, operation should be done without delay.

In cases with intermittent fever and mild jaundice haemolytic ictero- *Diagnosis* anaemia must be excluded. The absence of splenic enlargement, the *from haemolytic* direct positive van den Bergh reaction, bile in the urine, normal fragility *ictero-* of red cells, and a normal reticulocyte count will definitely exclude *anaemia* haemolytic jaundice. But even when signs of the latter disease are present, a stone in the common duct with a superimposed obstructive type of jaundice may be found owing to the great liability for pigment stones to form in the gall-bladder in the haemolytic disease.

(c) Medical Treatment for Stone in Common Bile-Duct

Medical treatment has a threefold object: (i) to relax the sphincter of *Aims* Oddi and favour the passage of the stone; (ii) to disinfect the bile and diminish cholangitis; and (iii) to increase the flow of bile and flush out the duct.

(i) To relax the sphincter of Oddi atropine has often been given but *Methods* with questionable benefit. The use of amyl nitrite is based on the fact that this drug has been shown to relax the lower end of the bile-duct and to cause a lower pressure within the duct as tested by a manometer. Morphine has the opposite effect from the point of view of relieving the pain in biliary colic due to a stone in the duct. Inhalation of amyl nitrite is therefore more valuable than opiates.

(ii) To diminish infection in the duct large doses of hexamine, up to 90 grains, three times a day, may be given, together with sodium bicarbonate and potassium citrate.

(iii) To increase the flow of bile, bile salts and a saline such as sodium phosphate may with advantage be given.

It must be emphasized, however, that when a diagnosis of stone in the

common bile-duct has been made, perseverance with medical treatment for more than a few weeks is altogether unjustifiable.

(d) Operation for Stone in Common Bile-Duct

Indications and contra-indications

If the operation is undertaken between acute obstructive attacks, when the jaundice has waned and infection is quiescent, the risk is slight and the results are most gratifying. When, however, deep jaundice is present, owing to complete biliary obstruction from an impacted stone, the patient is cholaemic, liver function is disorganized, the tendency to bleed excessive, and consequently the risk of operation considerable. Thus, whilst the operative mortality for cholecystectomy is 2 per cent, that for all cases of stone in the duct is 9 per cent.

Pre-operative measures

Pre-operative preparation of the patient is all-important and should aim at diminishing the two main risks of cholaemia and haemorrhage. To guard against the former, large quantities of fluid and glucose should be given, preferably by the continuous intravenous drip method. Some fifteen pints of 6 per cent glucose may be given in the 48 hours preceding operation, and, with this, 10 units of insulin every six hours should be given as in Umber's treatment of cirrhosis. To minimize the risk of haemorrhage, if deep jaundice is present, the intravenous administration of 5 c.c. of 10 per cent calcium chloride solution may be given for two nights before operation, and 30 c.c. of 30 per cent sodium citrate should be given intramuscularly just before operation. Better than either of these is a transfusion of 10 ounces of whole blood some hours before, and the same amount again some hours after, operation. It has been suggested that a vitamin C deficiency may be a factor in predisposing to haemorrhage in some of these cases and ascorbic acid has been given with apparent benefit (Illingworth). If liver failure threatens after operation, as indicated by drowsiness, dry tongue, and pale watery bile, the intravenous glucose drip is continued and a diathermy current is passed through the lower part of the thorax to raise the temperature of the liver as recommended by Crile.

Operation

Gas and oxygen anaesthesia should be used, especially if the patient is jaundiced. Through a Kocher's oblique incision, five inches long, the gall-bladder is exposed. It will usually be found small and fibrotic and buried in adhesions. The latter are freed by dissection and the dilated and thickened duct is brought into view. The duct and the head of the pancreas are palpated and a single mobile stone, if felt, may be manipulated into the supraduodenal portion of the duct, cut down on, and removed. If this is not possible the duct is opened in its supraduodenal portion between two stay sutures, stone-forceps are inserted and the calculus is felt for and extracted. It is very seldom necessary to open the duodenum and to cut down on the papilla. The hepatic ducts must be explored to ensure that no stone is left. A probe, followed by graduated bougies, is then passed down through the papilla into the

Dilatation of papilla

duodenum and the papilla dilated. Finally a tube should be stitched into the duct, which is drained to the surface. As cholangitis is a usual

accompaniment of stone in the duct, it is wiser to institute drainage
in practically every case. When much 'biliary mud' or 'sand' is present
in the duct gentle irrigation with physiological saline solution should
be used to cleanse the duct. The duct should be drained for 12 days *Drainage*
after operation. On removing the tube the opening closes spontaneously,
usually within 24 hours.

In cases in which jaundice is absent or slight the gall-bladder should *Removal or*
be removed; in the case of deeply jaundiced patients it is wiser to *evacuation of*
evacuate but to leave the gall-bladder, lest oozing of blood from the *gall-bladder*
raw liver surface endanger the patient's life. When the patient is
intensely jaundiced and cholaemic the minimum which will give relief
must be done. Unless the stone presents and can be removed without
trauma it is wiser merely to open and drain the duct with the least
possible disturbance of parts and reserve the removal of the stone or
stones for a second operation. The minimum exposure of viscera, the
gentlest of handling, and the most meticulous haemostasis are requisites
for success in all operations on cholaemic and jaundiced patients.

(e) Recurrence of Stone in Common Bile-Duct

In cases of pronounced cholangitis with muddy infected bile, biliary
sand and stones, an operation, even though it includes a thorough
clearance of the duct and removal of the gall-bladder, may be followed
by a recurrence of stone. A second and, in a few cases, a third operation *Need for*
on the duct may prove necessary. In such cases, if the patient will face *repeated*
up to further operation in spite of disappointment, the prospect of *operations*
eventual cure may be held out with confidence. Some of the most
completely successful results have followed repeated operations.

(2)—Obliterative Cholangitis

This fortunately rare malady presents one of the most difficult of
surgical problems. The patient, who may or may not have gall-stones
in the gall-bladder, suffers from a syndrome closely resembling that
described by Charcot for stone in the common duct. At operation,
however, no stone is found in the duct, which is small, thickened, and
fibrosed. Traced upwards it leads to hepatic ducts which may be similarly
thickened or may be found greatly dilated. On opening the hepatic duct
there is a rush of infected bile, laden with minute black calculi. It is
seldom possible to use the gall-bladder to anastomose to the stomach
as the disease almost invariably affects the common duct proximal to
the junction of the cystic duct. It may be possible to anastomose a
dilated hepatic duct to the duodenum either by direct suture or over
a rubber tube. The opening shows a tendency to narrow by sclerosis
and the operation may have to be repeated. The ultimate prognosis in
this condition is poor. For congenital obliteration see p. 361.

(3)—Carcinoma of Bile-Ducts

Primary carcinoma of the papilla of Vater is not uncommon; of the *Clinical*
ducts above the duodenum it is rare. The clinical picture resembles *picture*

closely that of carcinoma of the head of the pancreas—a slow, painless, and progressive development of jaundice, associated with loss of weight, strength, and appetite. The jaundice assumes the dark green or malignancy type rather than the rich yellow of the incomplete obstruction due to stone. Itching and a tendency to bleed are often prominent features as the jaundice deepens. If occult blood is found in the stools before there is any evidence of haemorrhage elsewhere an ulcerative lesion in the region of the papilla may be suspected. When the tumour, usually a scirrhous carcinoma, involves the duct below the entrance of the cystic duct, the gall-bladder dilates and forms a palpable swelling full of tarry bile. When the tumour involves the duct above the entrance of the cystic duct, the gall-bladder is collapsed and empty.

Treatment   Occasionally it is possible to extirpate the growth by resecting the duct or by implanting the stump of duct above the growth into the duodenum, but in every case it is necessary, as a first stage, to drain the duct above the growth until jaundice has subsided and the patient's condition is such as to stand a prolonged and tedious operation.

(4)—Congenital Cyst of Common Bile-Duct

Clinical picture   This rare condition, the aetiology of which is obscure, must be borne in mind when a patient, usually a young adult, presents a rounded, elastic, and cyst-like swelling in the epigastrium and right hypochondrium. The swelling may attain great size and contain several pints of clear bile-stained fluid. The patient may have discomfort but seldom pain and complains of fullness and a sense of oppression below the ribs. Transient and slight jaundice may be noted but is not a feature of the
Morbid anatomy   condition. When exposed at operation a large sac, with a thick tough opaque wall, lying between the liver above and the stomach and duodenum below, is exposed. When the sac is opened a large quantity of clear or slightly turbid fluid escapes, followed by definitely bile-stained
Treatment   fluid. The treatment consists of making an anastomosis between the opening in the cyst and the duodenum. This can readily be done and gives a symptomatic cure.

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GANNISTER DISEASE

See SILICOSIS

GARGOYLISM

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1.—DEFINITION

(Synonyms.—Dysostosis multiplex (typus Hurler); chondro-osteodystrophy
of the Hurler type; Hurler's disease)

551.] Gargoylism is a rare syndrome, which was first described by Hurler
and is characterized by cranial deformity, chondro-osteodystrophy, a
peculiar facies, clouding of the corneae, mental deficiency, and hepato-
splenomegaly. Although several incomplete cases (formes frustes) have
been observed, patients with the complete syndrome usually resemble
one another as closely as, for instance, typical mongols, and it appears
justifiable to distinguish the condition as a separate entity. In the
absence of conclusive knowledge of pathogenesis, the descriptive name
gargoylism has been applied to these patients, whose large heads,
facial appearances, and skeletal deformities suggest a resemblance to
gargoyles.

2.–AETIOLOGY

Gargoylism is congenital and often familial, although certain evidence *Familial* that more than one generation has been affected is wanting. The parents *Incidence* have in almost every instance been healthy; parental consanguinity has been recorded, but there are at present insufficient data to assess the aetiological significance of this factor. Both sexes are affected, the *Sex* condition having been recorded in two brothers, two sisters, and in a brother and sister. Although the clinical picture has frequently suggested a diagnosis of congenital syphilis or rickets, neither of these diseases plays any part in aetiology.

3.–PATHOLOGY

Knowledge of the morbid histology rests on the investigation of four cases only, and up to the present time no detailed examination of the osseous system has been made.

Tuthill described the brain of one of Hurler's original patients as an example of juvenile amaurotic idiocy complicated by the presence of tuberculomas.

From the close resemblance of the neurohistological change to that *Relation to* characteristically seen in juvenile amaurotic idiocy it has been suggested *diseases of lipoid* that gargoylism might also prove to be a disease of lipoid metabolism, *metabolism* and that possibly the hepatosplenomegaly might be accounted for on this basis (Ellis, Sheldon, and Capon).

Two further cases have recently been made the subject of detailed pathological study by Ashby, Stewart, and Watkin, who essentially confirm and extend Tuthill's findings; one of their two cases showed a unilateral hydrocephalus, a small tumour attached to the choroid plexus in both lateral ventricles, and extensive cortical atrophy of the left hemisphere.

Microscopical examination of the nervous system showed throughout *Microscopical* a characteristic alteration of the ganglion cells; the cytoplasm was *appearances of nerve cells* distended with what appeared to be a lipoid substance, the nucleus was dislocated, and the Nissl granules were reduced in number and grouped in one part of the cell. A different lipoid substance, thought to be composed of cerebrosides, was found lying free in the basal ganglia and elsewhere. The second case showed similar, although less advanced, changes in the nervous system. The intracellular lipoid was peculiarly resistant to solvents and corresponded closely to that described in Tuthill's case of gargoylism and in juvenile amaurotic idiocy. The authors considered that these findings provided strong confirmatory evidence that gargoylism was a disease of lipoid metabolism.

Examination of the reticulo-endothelial system, however, has not yet

shown any evidence of involvement comparable to that in Gaucher's and Niemann-Pick's diseases, and the hepatosplenomegaly cannot be explained by lipoid infiltration. In the two cases just mentioned the liver and spleen were admittedly not enlarged, but in my patient (see Fig. 122) there was gross hepatosplenomegaly. Splenectomy was performed and a section of liver taken for biopsy; the spleen, which was more than three times the normal size, did not show any abnormality except hyperplasia of the pulp, and the liver cells, which were well filled with glycogen, were not abnormal. In neither organ were foam cells or abnormal lipoids present.

Hepato-splenomegaly

Endocrine glands

Endocrine disorder has been suggested by the observation that the sella turcica has been enlarged in almost all the cases examined radiologically, and the pituitary showed a generalized hyperplasia in the one case in which it was examined after death. One of Ashby, Stewart, and Watkin's cases had an enlarged thymus, and both of their cases showed gross thyroid abnormality, one a retention of the foetal state with absence of colloid, the other atrophy of the secretory cells and fibrosis. It is as yet too early to assess the part played by the thyro-pituitary mechanism in the production of the syndrome.

Fig. 122.—Gargoylism in child aged 2 years, showing hydrocephalus, heavy features, wide-set eyes, coarse eyebrows, hepatosplenomegaly and flexion deformity of hips and knees (Author's case)

4.—CLINICAL PICTURE

The face is usually most strikingly abnormal; the features of even the youngest patients present a peculiarly heavy, unchildlike appearance reminiscent of the illustrations of the Duchess in 'Alice in Wonderland'. Whereas the hair is often silky, the eyebrows are almost invariably dark and coarse; the eyelids, nose, and lips are grossly thickened, a deep crease running on either side from the nose to the angle of the mouth. The bridge of the nose is depressed, the deformity being often associated with profuse purulent nasal discharge, and in some instances there is a moderate degree of hypertelorism. Distension of the scalp veins has been described, the frontal veins lying in deep gutters. The ears are sometimes set abnormally low; deafness is an occasional symptom.

Peculiar facies

A characteristic feature is clouding of the corneae, due to the presence of multiple congenital opacities. Examination with the slit-lamp shows these to be situated throughout all the layers, or in the deeper layers,

Clouding of corneae

of the corneae. Their presence usually renders examination of the fundi impossible. but none of the patients has been completely blind.

The skull varies considerably in size and shape and is commonly *Skull* enlarged. It has been described in different instances as hydrocephalic. scaphocephalic. acrocephalic (oxycephalic), and brachycephalic. Internal hydrocephalus was found at the necropsy of one case and by encephalography in two cases. The cranial sutures may be slightly separated or palpable as thickened ridges: in one instance the supra-orbital ridges were enormously over-developed. Radiological examination of the sella

FIG. 123.—Encephalogram showing gross dilatation of the whole ventricular system; sella turcica greatly elongated (Author's case)

turcica shows this to be greatly elongated: the clinoid processes may be defective or dislocated but do not appear eroded as by a tumour. (See Fig. 123.)

Some degree of lumbar kyphosis or deformity of the body of one or *Spine* more of the lumbar vertebrae is constantly present. A lateral radiograph shows a defect of the upper anterior portion of the affected body, producing an anterior hook-like process. (See Fig. 124.)

There is a limitation of extension of most, if not all, the joints, this being *Limbs* most marked in the hands. The patients can seldom stand completely erect, which adds to the deformity occasioned by the kyphosis. Radiological examination shows a peculiar and irregular chondro-osteodystrophy, resembling, if not identical with, that described by Brailsford, Morquio, and others. The glenoid fossae, the acetabula, and the heads of the humeri and femora are poorly and irregularly formed, and coxa

vara or valga deformity is present. All the bones are liable to show gross irregularity in structure and outline, this being most advanced in the region of the epiphyses, which may be irregular, delayed, or fragmented.

Thorax

The thorax is not usually deformed to any considerable extent but trichterbrust ('funnel chest') and expansion of the ribs have been described. The clavicles may be unusually massive.

Viscera

The liver and spleen are typically, though not invariably, enlarged and are smooth, firm, and not tender. The abdomen commonly appears distended, and inguinal or umbilical herniae are often present. The tongue may also be enlarged.

Mental state

The mental state has varied considerably in different cases; it is characteristically retarded but least so in the formes frustes of the disease. The patients are usually low-grade imbeciles, often not acquiring intelligible speech. In some cases there has clearly been rapid regression during later infancy.

Fig. 124.—Spine showing deformity of bodies of lumbar vertebrae
(Author's case)

In addition to dwarfism due to deformity there may be an extreme degree of infantilism (Ellis,

Infantilism   Sheldon, and Capon), but sexual maturity may be reached at the normal age (Ashby, Stewart, and Watkin).

5.–COURSE AND PROGNOSIS

Except in the less complete forms of the disease the patients are liable to die in childhood from intercurrent diseases. The condition is, however, compatible with survival to adult years. There is a tendency to progressive mental deterioration.

6.–DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

If the patients can be fully investigated clinically and radiologically, the character of the changes in the bones and their association with hepato-

splenomegaly and clouding of the corneae are diagnostic, and the facies
alone will often immediately suggest the diagnosis. The facies differs *Diagnosis*
from that of cretinism in that the features are altogether grosser, the *from*
cretinism
eyes are usually set widely apart, and the nasal bridge is depressed.
Rickets and congenital syphilis can be excluded radiologically and by
the serum reactions. Examination of the corneae will show that the
opacities are not due to interstitial keratitis.

7.—TREATMENT

Owing to the advanced changes in the central nervous system it is most
unlikely that any form of therapy will prove effective in the fully de-
veloped syndrome. Thyroid administration alone has been found of little
or no value, but the enlargement of the pituitary, the similarity of the
facies in some cases to that of infantile acromegaly, and the post-mortem
evidence of hypothyroidism suggest that further endocrine therapy may
be worth experimental trial.

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GASSING AND POISON GASES IN WAR

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Reference may also be made to the following titles:

BRONCHITIS AND BRONCHO-   BURNS AND SCALDS
 PNEUMONIA   RESUSCITATION
            SHOCK AND COLLAPSE

1.–INTRODUCTORY

552.] This article outlines the nature of certain agents used in chemical warfare and describes their action on the body. It also deals with the methods for treating the lesions they produce. and the defensive measures which may be adopted against gas attacks. Consideration has been limited to those gases which came into prominence during the War 1914 to 1918, with the exception of lewisite which was evolved in the closing phase of that war but owing to the cessation of hostilities was not used in the field. It is possible that further research may have resulted in the development of new compounds or in alterations in those previously used. In a future war, if cases of poisoning occur in which the signs and symptoms differ materially from those about to be described, it is probable that some new compound is in use, and the matter should be officially reported in order that steps may be taken to evolve appropriate new methods of prevention and treatment.

The classification adopted is based on the most prominent action of each agent on the body, and the gases have accordingly been grouped as vesicant, asphyxiant, lacrimatory, and sensory irritant.

2.–VESICANT GASES

553.] Vesicant gases include those chemical warfare agents which, in the solid, liquid, or gaseous state, damage the cells of the body with which they come in contact. Their action is essentially local, and the most characteristic manifestation is blistering of the skin. When the concentration and the duration of exposure are sufficient to produce an injury, the effect is an irritative response of the cells affected. This becomes evident, after a latent period, as an inflammatory reaction accompanied

Mode of action

by a progressive local oedematous infiltration which, in the case of the skin and mucous membranes, may raise the superficial epithelium and form blisters. The ultimate effect of the poison on the cells may be their complete destruction. These gases are exceedingly powerful in their action, but usually they produce minor casualties rather than death. Their most dangerous action is upon the respiratory system; in other parts of the body the general toxic effects are comparable to those of an ordinary thermal burn.

The only war gas of this group which has been used so far as an offensive weapon is mustard gas, which was first introduced by the Germans in July 1917, but since the War 1914 to 1918 others, such as lewisite, have been added to the group.

(1)—Mustard Gas
(a) Chemical and Physical Properties

Mustard gas was the name given to the chemical compound $\beta\beta'$ dichlorodiethyl sulphide, for which the formula is:

$$S\begin{cases} CH_2.CH_2Cl \\ CH_2.CH_2Cl \end{cases}$$

This compound is not chemically related to the oil of mustard, which belongs to a different group of chemical substances.

The manufacture of mustard gas does not present any great difficulties. Provided the necessary plant is available, large quantities can be prepared. In countries where the dye industry is highly developed it is easy to adapt the existing plant for the production of mustard gas, and, in addition, chemicals used in this industry can be utilized.

Physical properties In a chemically pure state it is a clear, almost colourless, heavy, and somewhat oily fluid with a faint odour resembling that of mustard or garlic. The boiling point is high, 217° C., and at 14° C. it becomes a white crystalline solid. The vapour pressure is low; hence it vaporizes very slowly at ordinary temperatures and is the most persistent of all the chemical warfare agents so far used. Subjected to high temperatures the liquid yields pungent vapours of high toxicity.

The commercial product contains impurities which alter its physical properties. In this form it is a dark-coloured heavy oily liquid with a much more pronounced odour and becomes a solid at a considerably lower temperature, about 7° or 8° C.

Hydrolysis In water hydrolysis takes place very slowly at ordinary temperatures and more rapidly at high temperatures. The compounds which result from hydrolysis are thiodiglycol and hydrochloric acid:

$$S\begin{cases} CH_2.CH_2Cl \\ CH_2.CH_2Cl \end{cases} + 2H_2O = S\begin{cases} CH_2.CH_2OH \\ CH_2.CH_2OH \end{cases} + 2HCl$$

Thiodiglycol is non-toxic, and hydrochloric acid in small quantities is harmless. Being heavier than water, mustard gas sinks to the bottom,

and there, at average temperatures, decomposition goes on slowly. The impurities in crude mustard gas impart to the water an acid taste and an unpleasant flavour. It is therefore unlikely that a water-supply which has been heavily contaminated would be used for drinking purposes.

In contrast to the relative insolubility of mustard gas in water it is *Solubility* freely soluble in many organic solvents, such as alcohol, carbon tetrachloride, and petrol, and readily dissolves in many oils, especially those of animal or vegetable origin. This latter property is responsible for its extraordinarily penetrative effect on animal tissues.

The stability of this compound is perhaps one of its greatest assets as *Stability* a chemical warfare agent. It may be slowly rendered innocuous by weathering and heat, and rapidly by chlorination, conveniently produced by the action of bleaching powder. Hypochlorites oxidize mustard gas to mustard sulphoxide, which is non-toxic: the interaction is extremely violent and, with undiluted compounds, produces great heat, which is sufficient to ignite the compound.

$$S \begin{cases} CH_2.CH_2Cl \\ CH_2.CH_2Cl \end{cases} + CaOCl_2 = SO \begin{cases} CH_2.CH_2Cl \\ CH_2.CH_2Cl \end{cases} - CaCl_2$$

Chlorine and other chlorinating agents, such as dichloramine-T, may be used to render mustard gas harmless. Compounds of mustard gas with two to four chlorine atoms added are non-toxic:

$$S \begin{cases} CH_2.CH_2Cl \\ CH_2.CH_2Cl \end{cases} + 2Cl_2 = S \begin{cases} CHCl.CH_2Cl \\ CHCl.CH_2Cl \end{cases} + 2HCl$$

A further important feature is the property which mustard gas possesses *Penetrating* of penetrating materials. As a liquid it will soak into articles much in *power* the same way as oil, but it differs from oil in that articles, such as grease-proof paper, which will withstand penetration of oil will not resist penetration by mustard gas. The vapour readily penetrates and adheres to clothing, more particularly woollen materials which contain natural fatty substances in the fibres. Ordinary clothing affords little or no protection and if worn after exposure is a source of danger. Rubber also is penetrated; hence thin rubber gloves, such as those used by surgeons, do not afford protection for any length of time.

(b) Efficacy as a Chemical Warfare Agent

Mustard gas has many features which make it prominent among the chemical agents used as offensive weapons in war. The odour is worthy *Odour* of special consideration, since recognition of mustard gas by the sense of smell is the most important means of detecting its presence. The odour is faint but characteristic and resembles mustard, horse-radish, or garlic, but its detection may be masked by the presence of more powerful odours such as are met with in time of war. The odour of crude mustard gas, although more pronounced than that of the pure compound, is, like the latter, not offensive. In an atmosphere laden with

Delayed action

the vapour the sense of smell soon becomes dulled, and the odour may cease to be appreciated after a short period of exposure. These are points of great importance, and they increase the value of mustard gas as an offensive agent, the dangers being underestimated in the absence of any strong odour. In addition, when the vapour or the liquid comes into contact with the skin or mucous membranes no immediate irritation is produced and, owing to the slowly volatile nature of the compound, a person may be splashed by small droplets and remain unaware of the contamination. These facts increase the risk of its non-detection.

(c) Methods of Release

When mustard gas is prepared for hostile purposes it is mixed with a solvent such as carbon tetrachloride, mainly to lower its melting point and increase its vaporizing properties. In the War 1914 to 1918 mustard gas was released entirely from shells. This was an expensive and not very efficient method of distribution, chiefly because most of the liquid was driven into the ground, where it ceased to be effective, and much was dispersed as a fine mist with consequent reduction in persistence. Since the War 1914 to 1918, with the development of aircraft, the methods of release which appear probable are the use of high-capacity containers or bombs, which will burst with the minimum of explosive violence and disperse the liquid on the ground. Dispersion can also be effected by spray from aeroplanes.

(d) Mode of Action

Several hypotheses have been advanced regarding the mode of action of mustard gas, but none entirely explains all the processes involved. The practical findings alone are dealt with here. Mustard gas, in much the same way as other chemical irritants, is essentially a cell poison the effect of which is localized to those cells with which it comes in contact. There is no evidence that it is absorbed and conveyed by the blood-stream to parts of the system distant from the primary lesion. Compared with other chemical irritants, the action of mustard gas resembles in some respects that of hydrochloric acid, but it is very much more injurious. A comparison can be made to an X-ray burn in the slowly progressive nature of the lesion and in the delay in healing. The con-

Toxicity

centration which is given as being injurious to the lungs is approximately 1 in 1,000,000 when breathed for 60 minutes. This indicates that contact with the vapour must be maintained for some time before an injury results. For example, if an individual wearing a respirator is exposed to a concentration of 1 in 1,000,000 for 15 minutes, and his contaminated clothing is then transferred to a second subject who wears it for a considerably longer time, the latter will develop injuries to the skin, whereas the former will not show any lesions. Detectable concentrations, if maintained for a period of time, which may be intermittent, will produce an injury.

(e) Morbid Anatomy

Lesions of the respiratory tract are the most important of all the *Lesions of* pathological changes. The entire respiratory tract from the nasal pass- *respiratory tract* ages to the alveoli may be affected, and the degree of injury may vary from a mild catarrh to an extensive necrosis and sloughing. Membrane formation, an important feature of the condition, causes mechanical obstruction, which in turn leads to emphysematous changes. The damage to the mucous membrane also favours the growth of organisms with the possible development of septic broncho-pneumonia. Casts from the trachea and bronchi consisting of necrosed epithelium may be coughed up. In the most severe cases an acute purulent capillary bronchitis develops and causes collapse of lung tissue and broncho-pneumonia.

Microscopically, the bronchiole is filled with fibrin and pus cells, and *Microscopic* its lining epithelium is completely destroyed. The peribronchial inflam- *changes* mation causes a characteristic ring of haemorrhage in the tissues around the bronchial tube, and infection first occurs in the alveoli in proximity to the inflamed bronchiole. In contrast to the asphyxiant chemical agents there is not any generalized pulmonary oedema. The later changes are those of a broncho-pneumonia with its typical patchy distribution, collapse of portions of lung tissue and more emphysema than in the earlier stages.

The skin may show all degrees of burn from a primary erythema *Effect on skin* followed by vesication up to the final stage of deep destruction with necrosis and sloughing. The stage of vesication is prolonged and progresses slowly, so that, if the patient should succumb within a few days of the exposure, the phase of necrosis will not be reached. Histologically the tissues are oedematous, and there is evidence of early damage to the blood-vessels. In contrast to a thermal burn the vessels are not thrombosed. At a later stage liquefaction of superficial cells follows and is accompanied by vascular and lymphatic congestion in the subcutaneous tissues. The lesion progresses slowly, ending in necrosis with consequent leucocytic infiltration. Healing is slow with formation of a parchment-like scar which is frequently surrounded by a pigmented zone. Pigmentation is usually marked, the colour being brown, purplish brown, or almost black. It may develop without preceding erythema and bears no evident relationship to the severity of the burn. The pigment is provided by the unusual activity of the chromophores in the basal layer of the epidermis, the corium being unaffected. It persists until the activity of the chromophores has subsided and the epidermic cells which they have supplied with pigment granules have reached the surface and been cast off. With the more severe degree of burn delay in healing is a conspicuous feature. The granulation tissue is unhealthy, oedematous, and bleeds readily. The devitalized tissue is very prone to septic invasion and injury from pressure.

The action of mustard gas upon the cornea and conjunctiva is very *Effect on eyes*

similar to its action on the skin. The degree of injury may vary from

Results of severe burns

mild degenerative changes to complete necrosis of the cornea. In patients who have been severely burned by the vapour, both the eyelids and the conjunctiva show an intense inflammatory reaction. The conjunctiva is swollen, oedematous, and bright red from injection of the blood-vessels. At this stage the injury to the cornea is not obvious and can only be detected by careful examination. When a greater degree of injury has occurred the conjunctiva in the interpalpebral aperture appears as a dead white band across the eye, as a result of coagulative oedema compressing the blood-vessels. The portions of the membrane which are protected by the upper and lower lids show at the same time marked

Chemosis

congestion of the blood-vessels. There may be also chemosis of such intensity as to result in the protrusion of the oedematous conjunctiva between the lids. Similarly the exposed part of the cornea is markedly affected. It loses its lustre, appears grey and hazy, and when viewed with a bright light and magnifying glass shows a blurred 'window reflex' and stippled surface. This contrasts with the protected parts of the cornea which retain their bright and smooth appearance. The constriction of the vessels on either side of the cornea may seriously interfere with the nutrition of this tissue, and secondary infection is liable to follow. Owing to the intense inflammatory reaction the pupil is contracted.

Secondary infection

At a slightly later stage, if secondary infection of the devitalized cornea occurs, corneal ulceration develops, and the subsequent spread of infection to the interior of the eye may lead ultimately to panophthalmitis.

Resolution

After a moderately severe degree of burning resolution is shown by gradual subsidence of the vascular injection and absorption of the oedema. This is accompanied by regeneration of the corneal epithelium, which regains its normal lustre. In very severe cases resolution is first apparent in those parts of the eye which have been protected by the lids. In this situation there is a gradual disappearance of the oedema and vascular congestion. At the same time the solid oedema in the interpalpebral aperture gradually becomes absorbed, and the blood-vessels in this area now become injected. At this stage there is a limited central band of vascular congestion, and the eye presents an appearance similar to that seen after very slight exposure to the vapour. The cornea now becomes smooth and regains its lustre, but, although it may show a clear light reflex on its surface, a few grey superficial nebulae may persist for some weeks. Ultimately the corneal epithelium is regenerated, its transparency returns, and unchanged visual acuity results.

During the War 1914 to 1918, although in the greater proportion of the mustard-gas casualties the eyes suffered, the vast majority of the cases were slight and of short duration. In this campaign, however, the methods used for the distribution of mustard gas were such as to produce injuries mostly from vapour. Ulceration of the cornea occurred in a few cases only, and panophthalmitis was exceedingly rare. The latter condition occurred mainly in cases in which the liquid was splashed in

the eyes. Permanent blindness immediately after the mustard gas lesions was a rare sequela.

Later sequelae which may develop many years (ten to fifteen) after *Late sequels* the injury consist of a red-veined marbled appearance of the conjunctiva, the result of a conjunctival fibrosis with injected vessels, often irregular in calibre, in the white fibrous tissue. In addition, a relatively insensitive condition of the cornea may occur. This is associated with a curious devitalized condition of the corneal tissue, which is liable to break down at intervals with the formation of ulcers, which heal only to form again elsewhere. Gradual scarring of the cornea and irregular astigmatism result, both causing very serious impairment of vision. It has been noted that these effects are much accentuated by residence in the tropics.

(f) Symptoms

When a totally unprotected individual is exposed either to the vapour or to a fine spray of mustard gas, immediate effects are not noticed. A faint smell can often be detected and may or may not be recognized as mustard gas, according to the presence or absence of other odours. The preliminary effects do not follow until after two or three hours. The first symptoms of which the patient usually complains are smarting and watering of the eyes, which rapidly develop into definite conjunctivitis, followed by symptoms simulating those of a common cold, accompanied by running from the nose with frequent attacks of sneezing. Nausea accompanied by retching, vomiting, and epigastric pain is not uncommon. As the condition develops, the conjunctivae become deeply injected and oedematous. The eyelids swell and finally close as a result of oedema, so that the individual is unable to see. The commonest mustard-gas casualty seen at the dressing stations in France was temporary blindness. Irritation of the respiratory tract now becomes more obvious and the voice gradually harsher until complete aphonia develops. Laryngeal irritation leads to frequent attacks of harsh dry coughing unaccompanied by expectoration. There is a dry and burning sensation leading to thirst.

Following this train of symptoms the lesions of the skin gradually *Progressive* become more apparent, and the erythema spreads and deepens in in- *lesions* tensity. The areas of the skin most affected are the exposed parts—the face and hands—and the moist areas, such as the axillae, groins, and genitals. Skin when hot and moist from perspiration is more severely affected than when cool and dry. In mild cases the condition may not progress beyond the stage of erythema, but in more severe cases the erythematous areas become covered with vesicles which quickly coalesce to form large blisters. After twenty-four hours the eyes are completely closed, and tears or muco-pus trickle intermittently down the cheeks. The pain in the eyes is intense and leads to constant restlessness. Severe frontal headache due to irritation of the frontal sinuses is common. Photophobia and blepharospasm are extreme, and any attempt to open the eyes for examination or treatment causes severe pain. At this stage,

apart from the pain in the eyes, the patients are moderately comfortable, as the skin burns at this time are practically painless.

Later symptoms

In the next twenty-four hours the condition is aggravated by the formation of blisters and oedema of the lax subcutaneous tissues, the genitalia in particular being almost always affected. From this stage onwards the main symptoms are referable to the respiratory tract. Finally the case becomes one of septic broncho-pneumonia or a condition of suppurating burns of the skin or a combination of both.

Cause of death

The commonest cause of death is the involvement of the respiratory system. The highest death-rate occurs at the end of the third or fourth day after exposure. A fatal result within the first twenty-four hours is extremely uncommon.

(g) Prognosis

Owing to the progressive action of the mustard gas when once it is absorbed, it is often difficult to estimate the ultimate degree of injury that may result.

In the milder degrees of skin burns the outlook is favourable; but, when extensive areas of skin are involved with destruction of the deeper tissues, prognosis must be guarded. In affections of the eye, unless the cornea is damaged, the prognosis is good. Ulceration of the cornea may result from exfoliation of the damaged epithelium or from an abrasion. In such cases there is a liability to infection and infiltration leading to permanent opacities, impairment of vision, and possibly total blindness. The subsequent history of some cases injured by mustard gas in the War 1914 to 1918 shows that a predisposition to recurrent eye affections is left. This is particularly evident in persons who are exposed to the irritation produced by wind, dust, and glare, more particularly in the tropics. The most serious results follow damage to the mucous membrane of the respiratory tract, as there is always the possibility of septic broncho-pneumonia.

Death-rate

The death-rate from all forms of mustard gas lesions during the period this gas was used (1917 to 1918) was low. Among the British troops in France it was less than 2 per cent.

(h) Prevention of Burns

Whether the contamination by mustard gas is accidental as in the case of research work or deliberate as in the event of war, distinct forms must be recognized, i.e. contamination by the vapour and by the liquid. The steps taken to prevent or alleviate lesions differ accordingly.

Contamination by vapour

Removal of clothing

In both vapour and liquid contamination it is essential to remove the clothing at the earliest opportunity on leaving the contaminated atmosphere. If the exposure has been to vapour, it may be presumed that the gas has penetrated the clothing and affected the skin. It is, therefore, necessary to remove from the skin any unabsorbed mustard gas, and this is most readily achieved by a bath and thorough washing with soft soap and water.

In the absence of facilities for bathing and if erythema has not de- *Bathing* veloped, the mustard gas may be neutralized by 'bleach'. The term *'bleach'* 'bleach' is used as a contraction of bleaching powder. the chlorinated lime of the British Pharmacopoeia which contains not less than 30 per cent of available chlorine. Stabilized bleaching powder. containing added quicklime, retains the available chlorine more securely than does the ordinary variety of 'bleach'. Both forms should be stored in closed containers, preferably in a cool place. As the unstabilized variety contains a small proportion of water it is liable to corrode metal containers. Bleach ointment is useful, but bleach preparations may irritate the skin and will certainly aggravate an existing erythema if they are not removed within a brief period. In fact bleach treatment either by an aqueous preparation or ointment (2 parts of stabilized bleaching powder to 1 of white mineral jelly) is only of real value when the application is made *immediately* after a short exposure to direct contamination with liquid mustard gas, but even in this case washing as indicated above may be equally efficacious.

The amount of unabsorbed mustard gas which remains on the skin after vapour-contaminated clothing has been removed is trifling. It follows, therefore, that practically no further degree of injury occurs after removal of the clothing. Although it is advisable to adopt the precaution of thorough washing with soap and water or the use of bleach when the clothes have been removed, it need not be anticipated that the degree of injury will be accentuated if these facilities are not available. In this latter event a dry rub down can be substituted for these procedures. The most important preventive measure is immediate removal of the contaminated clothing.

Contamination by liquid

In the case of contamination by liquid mustard gas the necessity for rapid removal of clothing and immediate preventive treatment is even more essential. If the removal of the liquid is delayed for five minutes in a temperate climate, and for a much briefer period in a tropical climate, vesication will not be prevented. In any event under the most favourable conditions an erythematous inflammation of the skin will inevitably result.

Immediate removal of the unabsorbed liquid is the first essential. In *Wiping to be* ordinary circumstances the site of contamination should be dabbed *avoided* with any absorbent material, but wiping the area should be avoided, as this method of removal will spread the liquid mustard gas over a larger area than the original site of contamination. If any solvents of mustard *Solvents to* gas are at hand, such as petrol, kerosene, or methylated spirit, the material *be used* for the removal should first be soaked in one of them, and successive applications of the solvent should be made. Care must, however, be taken to confine the solvent to the area affected and to safeguard the fingers of the operator.

The liquid can be neutralized by the application of some form of bleach

Neutraliza-tion　preparation. That most generally used is bleach cream—equal parts by volume of bleaching powder and water well mixed. When extensive areas of the body are involved the bleach can be conveniently applied by means of a large whitewash brush. The bleach should subsequently be washed off the skin; otherwise it will act as an irritant. Washing with soap and water has a limited application; more rapid removal by one or other of the methods outlined above is preferable in cases of gross contamination.

Protection of medical attendant　The treatment of mustard gas casualties is not without danger to the medical attendant, unless certain precautions are taken. In the first place, an appreciation of the characteristic odour of the gas is essential, so that contamination of the patient's clothes is recognized. Secondly, the persistent nature of the gas must be borne in mind and the fact that any of the wearing apparel of the patient, e.g. clothes and boots, may continue to be a potential source of danger, unless removed from the treatment room. Finally, the insidious method of action of the gas indicates the danger of remaining in a detectable concentration for any lengthy period unless a respirator and suitable protective clothing are worn.

(i) Treatment
Lesions of the skin

The treatment of lesions of the skin resulting from mustard gas is similar to that of thermal burns in general (see BURNS AND SCALDS, Vol. II, p. 723).

Erythema　In the early stages of diffuse erythema there is not any pain, and only a slight degree of irritation is experienced. The progressive tendency of the action of mustard gas influences the line of treatment in as much as each patient must be regarded as liable to suffer from a severe injury, the degree of which may not be indicated by the earlier signs. For this reason the skin should be cleansed with soap and water and the hair of the pubes and axillae clipped short in all cases. To allay the irritation which is often present in the early stages evaporating lotions may be used, or a lotion containing calamine and 1 per cent of tannic acid such as suggested by Mitchiner to relieve severe sunburn.

Prepared calamine	–	–	–	–	400 grains
Zinc oxide	–	–	–	–	400 grains
Tannic acid	–	–	–	–	100 grains
Glycerin –	–	–	–	–	1 fl. ounce
Water –	–	–	–	–	to 1 pint

To be applied at hourly intervals till irritation is relieved.

Experience during 1917 to 1918 showed that dusting powders and ointments are not to be recommended.

Vesication　When the erythema is progressing to vesication the inflamed skin becomes very fragile and is readily loosened by pressure or rubbing. It is therefore important that the affected skin should be protected

from trauma. Blistering of the buttocks and lesions of the genitalia, very common features of these cases, are better treated in bed.

Vesication commences by the formation of minute bullae which later coalesce to form large blisters. During their development the blisters are usually painless; but, when they have burst, the resulting raw surface is painful, more especially during the removal of the dressings. To relieve *Danger of* pain the administration of a general anaesthetic can be considered only *anaesthetics* when the gas has not damaged the respiratory passages. Local anaesthetics are not advised, as the sedative effect of opium or morphine may suffice.

Tense blisters should be opened under sterile precautions and raised epithelium removed. The area should then be carefully washed with soap and water, dried with a sterile towel, and swabbed with spirit. In the case of burns in the pubic region and axillae it is advisable to sponge ether over the area to remove grease and sweat.

Tannic acid treatment, as used in thermal burns, has been found to *Tannic acid* give very satisfactory results when the blisters are of a superficial char- *treatment* acter, but few opportunities have arisen since the War 1914 to 1918 for determining the effects of this treatment with deep and extensive burns associated with profuse exudation for several days.

Tannic acid in powder form does not deteriorate and keeps indefinitely *Storing the* if dry and stored in the dark, but in aqueous solution it rapidly becomes *solution* infected with moulds unless an antiseptic is added. The addition of mercuric chloride in a strength of 1 in 2,000 is harmless to the patient and will keep the solution free from moulds. It is convenient to keep the appropriate quantities of tannic acid and mercuric chloride either in powder or tablet form, so that, when they are dissolved in the requisite amount of water, a 2 per cent solution of tannic acid in 1 in 2,000 mercuric chloride results. These solutions of tannic acid should be stored in a cool and dark cupboard. The most favourable results follow the use of freshly prepared solutions. A 5 per cent solution of tannic acid containing 20 per cent of dettol does not deteriorate. For use it should be diluted with an equal quantity of warm water. The advantage of dettol is that it is non-toxic; its only disadvantage is that its application may be painful. Other combinations of tannic acid with an antiseptic added, such as amertan and tannafax, are available on the market. The choice of the antiseptic and, indeed, of any therapeutic agent for the treatment of extensive raw areas requires careful consideration owing to the rapidity with which absorption may occur.

The method of application is described under the title BURNS AND SCALDS, Vol. II, p. 724.

Recently, crude cod-liver oil has been used with promising results for *Cod-liver oil* the treatment of small burns. Lint soaked in the oil is applied to the *treatment* ulcerated surface, and this dressing, in addition to reducing pain owing to the absence of its sticking to the wound, accelerates the healing process.

In cases in which treatment has been delayed and necrosis and slough-ing of the skin have developed, immersion in an antiseptic is indicated. An antiseptic hip-bath is more particularly useful in the treatment of lesions affecting the genitals; care must be taken in the choice of antiseptic, the guiding principles being that it should be non-toxic and non-irritant. Experience during the War 1914 to 1918 indicated that the antiseptics used, including eusol, caused great pain. Continuous irrigation with physiological saline is often necessary.

Shock may develop as a result of extensive exposure to mustard gas but is rarely as severe as that following a thermal burn. The lines of treatment should be similar to those adopted in surgical shock (see SHOCK AND COLLAPSE).

When healing has taken place, a dry scaly condition of the skin fre-quently persists around the scarred area. This condition is also common in degrees of burn that do not progress beyond the stage of erythema, and Lassar's paste will be found to be a useful application.

Respiratory system

When the respiratory tract is involved the nasal passages should be douched at intervals with a warm alkaline solution such as sodium bicarbonate. Insufflation is not sufficiently thorough to reach the whole mucous membrane involved and is not satisfactory. In these cases a harsh persistent cough associated with laryngitis is common, and steam inhalations containing compound tincture of benzoin and menthol will give relief. Tracheitis is a troublesome complication which should be treated with antiseptic inhalations administered by a Burney Yeo's inhaler or some form of improvised mask. If broncho-pneumonia supervenes it should be treated on the usual lines (see BRONCHITIS AND BRONCHO-PNEUMONIA, Vol. II, p. 703).

Gastro-intestinal system

Gastro-intestinal symptoms may be alleviated by warm draughts of a weak solution of sodium bicarbonate.

Eye lesions

The most alarming results of exposure to the gas follow lesions of the eyes. Frequently there is temporary total blindness which causes the patient acute mental anguish. Reassurance that the sight has not been lost should be given at the earliest opportunity. The least severe affection resembles mild conjunctivitis, and should be treated by irrigation with sterile water or physiological saline. It is important after irrigation to instil into the eyes a few drops of sterile liquid paraffin or castor oil to prevent the eyelids from sticking.

In the more severe cases it is difficult to make any detailed examination owing to pain and blepharospasm. In such cases, if there is evidence of severe chemosis of the conjunctivae, it may be necessary to instil a few drops of a 1 per cent solution of cocaine hydrochloride in order to carry out the examination, but cocaine should not be used unless there are

special indications for doing so, as it may lead to exfoliation of the corneal epithelium. Manipulations must be made with the greatest care, as permanent damage may be caused to the eye from devitalization of the tissue. When the cornea is affected, in addition to frequent bathing the regular use of atropine is necessary. The instillation should be *Instillation* repeated sufficiently frequently to keep the pupils well dilated, and con- *of atropine* tinued until the cornea is completely healed. Secondary infections often follow damage to the cornea, owing to the lowered resistance of the tissues to bacterial invasion. If sepsis has occurred, a mild antiseptic such *Sepsis* as a 10 per cent solution of silver protein (protargol) or mild silver proteinate (argyrol) should be instilled at intervals. Infiltrating ulcers should be cauterized by the careful application of pure phenol, but care must be taken in the use of a caustic, as it may lead to extensive necrosis and perforation. Bandaging the eyes is not advocated, as any form of pressure should be avoided. An eye-shade or dark glasses should be worn to relieve the photophobia, but their use should be discontinued as soon as possible, irrespective of the wishes of the patient, as their prolonged use tends to accentuate neurasthenic symptoms.

General treatment

Finally, the general treatment requires consideration. In the more severe cases depression is prominent, and the patient tends to become a chronic invalid. For this reason, every effort should be made, by change of environment and encouragement, to restore the physical and mental fitness.

The majority of gas casualties during the period mustard gas was used in France (1917–18) were due to vapour contamination, and relatively few were caused by direct contamination with the liquid. Prolonged invalidism from the effects of the vapour occurred in a very small proportion of the cases, and most of the casualties from this type of contamination were returned to duty within two months. This contrasts with the prolonged convalescence necessary for the healing of the more severe burns caused by the liquid.

(2)—Lewisite

Lewisite—β-chlorovinyldichloroarsine ($CHCl:CHAsCl_2$)—is another *Chemical* example of a vesicant. It is liquid at ordinary temperatures, has a com- *properties* paratively low vapour-pressure, and is classed as a persistent gas; it hydrolyses rapidly in water and aqueous vapours, especially in the presence of alkalis. It is soluble in oils and in ordinary organic solvents. The odour is not strong and may be compared with that of geraniums.

Its action resembles mustard gas in that lesions result from contact with either the liquid or the vapour, but it differs from mustard gas in its more irritant effect and by the fact that its presence is more readily detected owing to its early sensory irritant effect. The vesicant action is powerful, and the blister fluid contains arsenic. There is less delay in the

appearance of injury than in burns due to mustard gas, and the lesion does not extend so deeply. The healing process also contrasts with that in mustard gas injuries, as ulceration is not so prolonged and indolent. The treatment is similar to that of a mustard gas injury.

Results of animal experiments   Experience of lewisite is limited to laboratory investigation, as it was not used during the War 1914 to 1918 and was not fully described until after its close. Experiments on laboratory animals have shown that the agent is absorbed through the skin, as arsenic has been demonstrated during life in the urine and after death in all the tissues of the body.

3.—LUNG IRRITANT (ASPHYXIANT) GASES

(1)—Chemical and Physical Properties

554.] The commoner asphyxiant gases that have been used in chemical warfare are chlorine, phosgene, and chloropicrin, and of these phosgene is the most important.

Phosgene   Phosgene ($COCl_2$) is a clear liquid, with a boiling point of 8·2° C., and, therefore, unless under pressure, is a gas at ordinary temperatures. The odour is characteristic and can be readily detected, resembling that of musty hay. In contact with moisture phosgene is very easily hydrolysed, forming hydrochloric acid and carbon dioxide.

Chlorine   Chlorine is a yellowish-green gas, heavier than air and far more irritant than phosgene to the respiratory passages.

Chloropicrin   Chloropicrin (CCl_3NO_2) in the commercial state is a yellowish liquid and is semi-persistent. Compared with chlorine and phosgene it causes greater sensory irritation of the respiratory passages and has a more marked lacrimatory action. It is more deadly than chlorine, but must be inhaled in a distinctly higher concentration than phosgene to cause severe pulmonary oedema.

The gases of this group can be released singly or in combination. It is sometimes impossible to define the exact agent which is being used, and a diagnosis can go no further than decide that the gassing is by a pulmonary irritant. Of the three agents mentioned phosgene is of outstanding importance owing to its extraordinarily toxic nature.

(2)—Mode of Action

Effect on lungs   These chemicals are usually dispersed in the gaseous state and exert their greatest effect on the epithelium and walls of the capillary vessels of the lobular bronchioles and alveoli. It is characteristic that the damage to the pulmonary tissues is generally not conspicuous until some hours have elapsed after the exposure. The predominant effect is a gross exudation of fluid into the alveoli, associated with inflammatory and necrotic changes in the mucous membrane of the bronchial tubes, acute emphysema, and capillary obstruction due to thrombosis or the formation of strands of fibrin. Laboratory investigation has shown that immediate death may occur when high concentrations of these gases are

inhaled, the fatal result being due to acute asphyxia caused by pulmonary *Causes of* stasis. In these cases the oedema of the pulmonary tissues may be slight. *death* As a general rule, however, acute pulmonary oedema is the characteristic symptom. The concentration of gas which will cause this result differs with the various agents, phosgene and chloropicrin exhibiting a greater toxicity in this respect than chlorine. Although in severe cases death may be due to acute pulmonary oedema, rapid recovery is a striking feature if the patient can be tided over the more acute asphyxial condition.

In addition to the effects which these gases produce in the lungs they also irritate the mucous membrane of the trachea and bronchi, pro- *Effect on* ducing congestion and necrosis of the epithelium, which lead to the *trachea and* *bronchi* formation of an inflammatory exudate. This inflammatory action varies in severity according to the different gases. For example, phosgene may induce such a degree of pulmonary oedema as to cause death without the production of any definite changes in the mucous membrane of the air tubes, except perhaps in the smallest bronchioles. On the other hand, the pulmonary oedema resulting from chlorine or chloropicrin is always accompanied by very definite inflammatory changes in the mucous membrane of the upper air-passages. This distinction is relative, as commercial phosgene has well-marked irritating properties.

(3)—Morbid Anatomy

(a) Lungs

Macroscopic appearances

At necropsy the lungs are so distended with fluid that they fill the thorax. They are uniformly bluish in colour with patches of emphysema which may extend along the visceral pleura as chains of little bubbles. Occasionally the emphysematous process may extend into the mediastinum and the subcutaneous tissues at the base of the neck, leading to surgical emphysema. Extensive emphysema, however, only occurs in chlorine poisoning.

In the early stages of pulmonary oedema there is an accumulation of fluid in the interstitial tissue of the lung, accompanied by distension of the lymphatics. At a more advanced stage there is an exudation of fluid into the alveoli, and the entire lung becomes involved. The degree of oedema varies in different parts of the lung, being dependent upon the lymphatic drainage. In parts the oedema is solid, while in other areas it is slight.

Microscopical appearances

All the pulmonary tissues show oedema, although the distribution of *Oedema* the oedematous process is irregular. The oedema fluid may contain desquamated alveolar cells and extravasated blood corpuscles. When the alveoli are completely filled with fluid the capillaries are greatly congested, but when the exudation of fluid is less, and particularly in the emphysematous patches, the congestion is not so intense. The

oedema is presumably due to the direct effect of the gas on the cells
lining the alveoli and the endothelium of the subjacent capillaries, but
whether this fluid, which is highly albuminous, should be regarded as a
product of an inflammatory reaction or as due to increased permeability

Necrosis

of these cells, if not to actual gross leakage, is uncertain. Necrotic
changes in the epithelium of the smallest bronchial tubes and some

Capillary
thrombosis

desquamation of the cells are usually evident. Capillary thrombosis in
the more severely damaged parts of the lung is not uncommon, and this
tendency to capillary thrombosis may occasionally be evident in other
parts of the body; for example, petechial haemorrhages are sometimes
seen in the cerebral cortex. These are not the result of embolism but
follow a local capillary thrombosis caused by damage to the vessels
resulting from oxygen deficiency.

(b) Circulatory System

There is venous stasis, all the large veins being engorged with blood.
The heart, particularly the right side, is usually, though not invariably,
distended, and petechial haemorrhages may be visible under the endo-
cardium.

(4)—Symptoms

The more serious cases of poisoning by the lung irritants may be
grouped clinically according to their mode of onset. There are three
types: (a) acute with violent onset, which usually causes the blue type
of asphyxia with intense venous congestion; (b) acute with insidious
onset, responsible for the pallid type of asphyxia with circulatory
failure; (c) the chronic type which results from repeated or prolonged
exposure to very low concentrations; these cases are not observed in the
field but have only been seen among workers in filling-factories.

(a) Acute Cases with Violent Onset

Chlorine

This type is best exemplified after exposure to chlorine. The character-
istic symptoms are coughing, choking, and gasping for breath. Death
does not usually occur until after the lapse of several hours, so that in
the field, provided conditions permit, there is generally time for evacua-
tion of even the worst cases. Soon after the initial coughing, and perhaps
retching, complaint is made of pain in the chest. A deep breath cannot
be taken, the chest feels incapable of expansion, and every effort to
breathe increases pain. Expectoration may be profuse, accompanied by
foaming at the mouth, or may be very slight, with relatively little cough.
Vomiting is rare, even in the worst cases. Headache and intense sense
of fatigue in all the limbs often cause great prostration. As the oedema
in the lungs develops, the breathing becomes rapid and panting but of a
characteristically shallow type comparable to that of a child suffering
from broncho-pneumonia. The ears, lips, and progressively the whole
face assume a cyanotic bluish-red tint, and in pure chlorine-gassed
cases this deepens to the plum type of cyanosis associated with venous

distension. Usually the patient is fully conscious and complains chiefly of headache and pains in the chest: he turns restlessly from side to side in extreme discomfort, and his hurried breathing is interrupted from time to time by short bursts of coughing and of expectoration. This blue type of asphyxia is associated with a full strong pulse at the onset, although later the pulse may fail and the asphyxia change to the pallid type.

(b) Acute Cases with Insidious Onset

In phosgene poisoning the stage of full venous congestion and deep *Phosgene* plum-coloured cyanosis is often absent, and the patient passes rapidly into a state of circulatory collapse, with a feeble flickering pulse of *Collapse* more than 120. The skin is cold and clammy, the face assumes a leaden hue, and the colour of the lips and lobes of the ears testifies to the asphyxial cyanosis. Persons who have been exposed to this gas are often able to carry on their work for an hour or two with only trivial discomfort. Symptoms, however, then set in and rapidly become accentuated, the patient passing into a condition of collapse with increasing oedema of the lungs which may progress to a fatal issue. This course of events is illustrated in a minor degree when persons who have been exposed to a low concentration of the gas at first do not complain of any effect but later become exhausted and breathless on exertion.

When pulmonary oedema sets in, the patient becomes restless, often *Oedema* semi-delirious, and the skin, at first dry and hot, becomes cold in the final collapse although not usually damp with perspiration. The pulse is rapid and small in volume, and the breathing is of a hurried shallow panting type, often accompanied by tracheal râles.

If there is evidence of pulmonary oedema, any surgical operation, even of a minor description without anaesthesia, is attended with great risk owing to the possibility of aggravation of the pulmonary condition.

Both the blue and the pallid types of cases have this one feature in *Changes in* common, that the colour of the blood indicates a grave deficiency of *blood* oxygen. In all cases of poisoning by acute lung irritants concentration of the blood occurs in the acute stage. The percentage of haemoglobin in the more severe cases may be extremely high with a corresponding increase in the red cell count, but in the milder cases this does not occur. In cases of poisoning by chlorine this change in the blood is evident immediately after the gassing, whereas after exposure to phosgene several hours usually elapse before the concentration of the blood reaches its maximum. This phenomenon depends on the loss of fluid due to the pulmonary oedema, on loss of fluid into the tissues as a result of shock, and probably also in some degree on the anoxaemia which raises the percentage of haemoglobin. In many cases the blood will scarcely flow from a cut vessel.

The rapidity and relative shallowness of the breathing that characterize *Breathing* the severe cases are the result not only of interference with the gaseous interchange but also of an exaggeration of the normal vagus reflex. This

type of breathing occurs in some cases during convalescence for the same reason.

Blood-pressure

The systolic arterial pressure always tends to be subnormal and the diastolic pressure high.

Circulatory failure

According to some authorities the circulatory failure can be explained by the local action of the pulmonary irritants on the tissues with which they come into immediate contact. It is thought that early circulatory failure is caused partly by pulmonary oedema affecting gaseous interchange and impeding circulation and partly by shock. Clinicians during the War 1914 to 1918 inclined to the opinion that cases of early collapse so common with phosgene could not be attributed to asphyxia alone, and suggested that phosgene might have a direct effect upon the heart and circulation. But the pathological and experimental evidence is against this latter view.

Delayed symptoms

A noteworthy feature of poisoning by the lung irritants is the delay which may occur in the onset of symptoms. Respiratory distress may not be immediately evident, and pulmonary damage may not become obvious for several hours after the inhalation of the gas. In such cases the sequence of events may present the following variations: (i) sudden death, without premonitory symptoms, may occur during the first day but is exceptional; (ii) pulmonary oedema in its most severe form may gradually supervene, even when the patient is at rest in bed; (iii) after an interval of a few days, during which there is no evidence of poisoning, the following symptoms may appear: vomiting, abdominal pain, shortness of breath, and fatigue. Though these symptoms may be associated with cardiac distress and a slight pyrexia, the condition does not usually call for anxiety. Many of these cases of delayed poisoning would not occur if the necessity of enforcing rest for twenty-four hours after the exposure to the gas was realized.

(c) *Chronic Types of Poisoning*

Factory workers

This form of poisoning is encountered among factory workers who are repeatedly exposed to low concentrations of phosgene or chloropicrin. Such persons become increasingly susceptible to the poisonous effect of these gases and ultimately suffer from general debility, dyspnoea, and recurrent attacks of asthma associated with a rapid pulse on exertion. Pulmonary oedema, however, does not as a rule occur as the result of chronic poisoning.

(5)—Physical Signs

In the early stages the percussion note is usually resonant, but on auscultation fine râles may be heard on deep inspiration chiefly in the axillae and over the back and side of the chest. At this stage, however, the physical signs are usually of little assistance either in estimating the degree of injury and the extent of pulmonary oedema or in forming a prognosis. The most useful points to note in this connexion are the colour of the patient and the pulse and the character of the respirations.

As the signs of oedema increase, which they may do with extreme rapidity, loud liquid râles and bubbling sounds are audible all over the chest. When the pulmonary oedema is well established there may be copious expectoration of frothy plum-coloured sputum which is highly albuminous and contains traces of blood. When inflammatory complications supervene the case exhibits the usual physical signs of a bronchitis, pleurisy, or broncho-pneumonia.

(6)—Prognosis

If the patient survives, recovery from pulmonary oedema, even in its most serious form, should be complete in four or five days. The occurrence of broncho-pneumonia is not common with the phosgene type of irritants. Complications, when they do occur, are more frequent when there has been previous lung trouble. When once the acute stage is passed, recovery from poisoning with the lung irritants is, as a rule, rapid and complete.

(7)—Treatment

The first essential is to determine if the person seeking treatment has really inhaled the gas. Experience has shown that in addition to genuine cases some highly strung individuals labour under the delusion that they also have been gassed. Conversely, others who have inhaled lethal doses *Difficulties* of the gas may require to be persuaded that treatment is necessary. The *in diagnosis* absence of two of the most readily determined signs of early gas poisoning, irritation of the upper respiratory passages and respiratory distress, render a decision difficult in the case of phosgene gas.

Some points are useful in coming to a conclusion. In doubtful cases careful interrogation may elicit the information that some unusual smell and taste was noticed. Even exposure to low concentrations of gas will alter the taste of tobacco smoke and may cause vertigo, lacrimation, and epigastric pain. Deep inspiration may provoke attacks of coughing and pain in the chest. In any event, if doubt exists the case should be treated as one of potential poisoning and the patient should be carefully transported and should not be allowed to exert himself in any way. Neglect of these precautions at this stage may lead to irreparable damage. If, however, symptoms have not appeared after the lapse of forty-eight hours, supervision may be relaxed.

In the acute stage rest is the chief essential. Any undue muscular exer- *Complete* tion tends to accentuate the pulmonary oedema and to increase the *rest essential* consumption of oxygen. If there is extreme restlessness morphine sulphate $\frac{1}{6}$ grain may be given once as a sedative, but the dangerously depressant action of this drug on the respiratory centre must be borne in mind. Transportation, if necessary, should be by stretcher, and the patient should be kept warm. Warmth lessens shock and by preventing shivering, which entails muscular movements, diminishes oxygen consumption. Phosgene being a non-persistent gas, it is not necessary, as a rule, to remove the patient's clothing before removal to hospital. These

cases must be treated as bed patients and must not be allowed up for any reason. Rest should be absolute until cyanosis and all symptoms have disappeared.

Treatment of cyanosis   Cyanosis is the chief indication of pulmonary oedema, and oxygen should always be administered to cases exhibiting the blue or the pallid type of asphyxia. It should be given continuously over a long period by some special apparatus, such as the Haldane mask or a nasal catheter. The minimal current of oxygen which will suffice to keep the patient's face pink should be used. Oxygen may also be given to the milder cases, but in a national emergency the supply of oxygen may not be unlimited, and there is also the question of the transportation of cylinders. Expectoration may be encouraged by some postural device. During the War 1914 to 1918 artificial respiration by Schäfer's method was found to be of value in expelling fluid from the lungs in a few semi-comatose cases, although great care was required in its use (see Vol. IV, p. 238). The induction of vomiting is also helpful in emptying the lungs but may produce exhaustion. Pain in the stomach will often be alleviated by doses of sodium bicarbonate. Thirst is constant, and the patients should be allowed to drink freely.

Venesection   In all cases of blue cyanosis with full pulse venesection should be performed and 15 to 20 fluid ounces of blood removed as early as possible. For the serious cases of early collapse with greyish pallor and rapid thready pulse venesection is not advisable. Some German workers used intravenous administration of 20 per cent glucose or physiological saline solution, but the results were not encouraging. British workers did not use saline transfusions, as it was feared that the immediate result might increase the pulmonary oedema and final asphyxiation.

Morphine dangerous   There are no drugs of any especial value that can be used in this condition. Atropine is not of any value, and morphine is dangerous and should only be used in special circumstances to control restlessness. Attempts to neutralize the gas by the inhalation of ammonia yielded disappointing results. Ether was used by the French for the relief of pain and respiratory distress.

Cardiac stimulants   Many different cardiac stimulants, such as brandy, pituitary (posterior lobe) extract, or camphor, have been used, the best being oxygen.

During the first two or three weeks of convalescence patients who have suffered from pulmonary oedema should be given opportunities for resting during the daytime between periods of exercise. In the event of a persistent high pulse-rate periods of exercise should be diminished. In the later stages of convalescence exercises should be carefully regulated.

4.–LACRIMATORS

555.] The lacrimatory gases may be released either as liquids or solids and are, in the same way as the sensory irritants, used as harassing agents. Lacrimatory properties are common to many chemical com-

pounds and appear to be associated with the presence of a halogen group. Examples of lacrimatory gases are (1) ethyliodoacetate (K.S.K.), $CH_2I.COOC_2H_5$; (2) bromobenzyl cyanide (B.B.C.). $C_6H_5.CHBrCN$; (3) chloroacetophenone (C.A.P.), $C_6H_5.COCH_2Cl$. The respirator gives complete protection, and apart from contact with a lacrimator in the liquid state, when it will act on the body like other corrosive chemicals, the effect of these gases upon protected persons may be regarded as of little importance medically. In low concentration, in either the gaseous or particulate state, when no protection is available their effect is to produce almost immediate watering of the eyes. In higher concentrations they cause in addition irritation of the eyes, associated with spasm of the eyelids, so that the individual cannot keep his eyes open. There may be also a slight sensation of tightening or stinging of the skin of the face, burning sensation in the throat, and discomfort in the chest.

These symptoms disappear with dramatic suddenness when the individual withdraws from the poisonous atmosphere or adjusts the respirator, and the redness and swelling of the eyelids and the injection of the conjunctivae usually disappear in a few hours.

No treatment other, perhaps, than simple lavage of the eyes is necessary. *Treatment*

5.–SENSORY IRRITANTS

556.] The sensory irritant poisons are arsenical preparations and have been used in warfare as harassing agents. These preparations may be regarded as substitution products of arseniuretted hydrogen (arsine), the hydrogen being replaced by chlorine, bromine, cyanide, and phenyl or ethyl radicles. This alteration in chemical composition masks to a large extent the ordinary poisonous properties of arsenic, and results in the compounds having as their main effect that of irritating intensely certain sensory nerves. Most of these compounds are solids at ordinary temperatures. Three typical examples are (1) diphenylchloroarsine (D.A.), $(C_6H_5)_2AsCl$; (2) diphenylcyanarsine (D.C.), $(C_6H_5)_2AsCN$; (3) diphenylaminechloroarsine (D.M.), $C_6H_4\big<\!\!\!\begin{smallmatrix}AsCl\\ NH\end{smallmatrix}\!\!\!\big>C_6H_4$. The sensory irritants have been dispersed in the form of particulate clouds, usually by heat, from generators. In the form of an invisible vapour they are effective in much lower concentrations than any of the other chemical warfare agents. Since the irritant clouds consist of actual particles, the *Respirator requires filter* respirator must be fitted with a filter, as charcoal is ineffective for their removal.

An unprotected person subjected to low concentrations of any of these compounds suffers, after a short period of delay, slight and transient nasal irritation. In higher concentrations there is repeated sneezing, *Symptoms* and burning pain in the nose, mouth, throat, and gums, followed by

salivation, lacrimation, pain, and a feeling of grit in the eyes, accompanied by copious watery discharge from the nose, frontal headache, and a sensation of tightness and pain in the chest. There may also be pain in the stomach and a slight burning or sensation of tightening of the skin of the face. Occasionally there may be nausea, retching, and vomiting. Sometimes also there may be giddiness, and some patients lose consciousness and remain comatose for several hours, and others without losing consciousness pass into a lethargic state for 12 to 24 hours. The pain and misery produced by these compounds may be most intense, and some individuals suffer great mental distress.

The symptoms, unlike those produced by the lacrimators, do not diminish as soon as the respirator is correctly adjusted or the individual leaves the poisonous atmosphere, but they may tend to increase before

Recovery they subside. On removal of the patient from the poisonous atmosphere the symptoms subside within twenty-four hours, and almost all patients recover within forty-eight hours. The condition seldom demands hospital treatment, and even in such cases convalescence is rapid. During the

Sequelae War 1914 to 1918 some rare sequelae were vague sensory and motor disturbances which were considered to be functional in character, although a final conclusion as to the true nature of these phenomena was not reached.

Contamination of water Water from shell-holes is liable to become contaminated by these arsenical compounds and, if used for washing purposes, may cause sensory disturbances of the skin unaccompanied by inflammation. Drinking water so contaminated causes gastro-intestinal irritation. No fatal cases have been recorded as occurring among humans as a result of poisoning with these gases.

Recognition of exposure to the sensory irritants is possible from the history of the onset of the symptoms, especially nasal irritation, sneezing, lacrimation, and nausea. Giddiness, lethargy, irritability, and perhaps loss of consciousness may also result.

Treatment As a general rule treatment is unnecessary, but in the early stages intense pain may be relieved by inhalations of chloroform. Inhalation of ammonia, insufflation of a 2 per cent solution of sodium bicarbonate, and gargling and washing out the eyes with warm water give relief. Treatment other than this is on general lines and during convalescence should be directed to improvement of the general condition. The mental disturbance is best met by suitable environment.

6.—DEFENSIVE MEASURES

(1)—Use and Limitations of Gas

557.] Defence against the agents used in chemical warfare is a very complex problem and, although general guidance can be given regarding the methods that can most usefully be adopted, the success of such efforts must ultimately depend on the active and enlightened collabora-

tion of each member of the community in an attacked area. In so far as the medical profession is concerned, the use of gas as an offensive weapon has opened up a new field of casualties which calls for specialized treatment. It has also raised many problems the solution of which is beset with great difficulties, for example, the protection of personnel handling the casualties, de-contamination of clothes, stretchers, and buildings, and a host of other subsidiary questions.

Towards the end of the 1914 to 1918 War, despite the fact that chemical warfare was in its infancy, the problems of the subject had already become very complicated. It can be anticipated that in the intervening years improved methods of liberating these agents have been developed and, further, that the combination of gas with high explosive and incendiary substances is likely to be encountered in the future. It will be evident, therefore, that the position regarding chemical warfare is not static and that any measures that may be advocated at present will require modification from time to time to meet new developments. This section does not, therefore, purport to deal with the subject in more than a general way.

The term gas is loosely used in connexion with chemical warfare and may refer to substances which are gaseous, liquid, or solid. All these chemical agents exhibit their most marked physiological effect upon some particular tissue or system of the body. Protective measures will consequently depend on the physical state of the gas and on the tissue or system of the body involved.

War gases are usually divided into two main groups, persistent and non-persistent. The term persistence signifies that the agent remains for a prolonged period physiologically active and, therefore, capable of producing its injurious effect. A non-persistent substance is one which is rapidly converted into a vapour or a particulate cloud. If the effective concentration is not immediately harmful, its action is soon decreased by wind or sun. A persistent gas, on the other hand, is generally in liquid form and vaporizes slowly and, therefore, maintains a physiologically active gaseous concentration for a considerable period of time. *Persistent and non-persistent gases*

The successful use of any gas depends on maintaining an effective concentration over a given area for a sufficient length of time. This is influenced principally by meteorological conditions, the nature of the soil, and topographical features. *Factors governing successful use of gas*

With regard to meteorological conditions, the most favourable for the liberation of gas are a wind of low velocity, a moderate temperature which is slowly decreasing, slight humidity, and the absence of bright sunlight. These factors all occur more often at night, and it is also in the hours of darkness that there is a greater likelihood of a surprise attack. *Influence of meteorological conditions*

Wind of low velocity, about five miles an hour, is particularly favourable for the use of gas, in contrast to a wind of high velocity, greater than twelve miles an hour, which disperses non-persistent gas rapidly and decreases the effectiveness of a persistent gas by assisting evaporation. A moderate temperature is generally more favourable than either *Wind*

Temperature

a high or a low one, as it assists vaporization of all kinds of gases without seriously affecting persistence. At low temperatures mustard gas becomes a solid, and this may render its presence difficult to detect. Its chemical composition, however, is not destroyed when it is frozen, and it becomes effective as soon as it resumes the liquid form. In hot weather the persistence of mustard gas is reduced, but under such conditions high concentrations are likely to occur in the vicinity of contaminated areas owing to its rapid vaporization. Moisture in the atmosphere, when there is little wind, assists the formation of a gas cloud and tends to keep it low, but heavy rain has the effect of destroying or removing gases, although this may not always be the case. In any weather in which it is possible for aircraft to fly gas may be released from the air.

Humidity

Soil

The nature of the soil has also an important bearing on the effectiveness of a persistent gas. Should the ground be soft and dry, liquids are absorbed and the possibility of injury from direct contact with the free liquid is reduced. This contrasts with the persistence of free and unabsorbed liquid which may remain for a considerable time on soft wet ground. In such circumstances contaminated mud is more liable to be picked up and carried on boots, and if these are worn in an enclosed space, such as a room or dressing station, a concentration of gas capable of producing casualties may result. Liquid gas penetrates into hard ground slowly and, when liberated on such a surface from containers which burst either by force of contact or by detonation, is scattered over a large area. Contaminated bricks and other absorbent hard materials favour persistence.

Contaminated mud

Topography

Topographical features must also be taken into consideration, as the concentration of gas which it is possible to maintain varies according to whether the gas is liberated in a built-up area, a heavily wooded area, or in open country. In built-up areas, owing to the screening effect of buildings, or in other sheltered places, such as woods or sunken roads, liquid gas persists longer and non-persistent gas disperses more slowly than in less sheltered areas.

Concentration

The concentration necessary to produce a lethal effect varies with the different types of gas, each having its own effective limit. Unlike the others, mustard gas has a cumulative action and, provided the concentration is sufficient to make its characteristic odour perceptible, is capable of producing casualties. A further factor which enters into this question is the length of time of exposure to the agent. The lower the concentration, provided that it is within its effective limit, the greater the length of time the gas will take to produce its characteristic effect.

Non-persistent gases

Non-persistent gases are unlikely to be effective unless the element of surprise is present and the maximum concentration of gas is rapidly produced. Even with a maximum concentration, such as may be produced under war conditions, the gas will not immediately give rise to casualties unless it is deeply inhaled.

Persons trained to detect gases and accustomed to the use of the

respirator should have time, therefore, to give the alarm. If panic can be prevented among a civilian population, few casualties should be expected from this type of gas.

On the other hand, when persistent gas is used, the object is not necessarily to aim at obtaining the maximum concentration but, rather, to spray the substance on a living target or to scatter it in adequate amount over as large an area as possible, so that in virtue of its persistence it will give off its toxic vapours over a prolonged period of time and produce a harassing effect. With non-persistent gases the physiological effect is immediately harmful, but in the case of mustard gas, excluding direct contact of the body with the liquid, contact with a detectable concentration of the vapour must be maintained for a period of time before an injury will result. *Persistent gases*

It is important to realize the enormous amount of gas which must be liberated in the open to obtain a concentration that will produce injurious effects. This in itself is obviously a great limiting factor. All gases in use at present can be detected by the senses, and few can be liberated in sufficient concentration to exert a lethal effect. Those which can be so used must be liberated in a very high concentration. Even if this high initial concentration is obtained, it is very difficult to maintain, as the meteorological factors already mentioned exert an important influence. If the element of surprise can be overcome, non-persistent gas is unlikely to produce casualties among those who have been trained in anti-gas measures. The defensive schemes advocated by the Air Raid Precautions Department of the Home Office, together with an efficient respirator, should materially minimize the possible effects of gas attacks. A more difficult problem concerns the protection which can be afforded to infants and infirm people. This aspect of the question is under investigation. *Limitations of gas* *Anti-gas measures*

Protection against the highly persistent mustard gas is a more complicated problem. The difficulty may not be so great in the early period of an aerial attack, when fresh and clean materials are available for decontamination in organized centres, but is likely to be accentuated in prolonged and repeated attacks, more particularly when mustard gas is being used in combination with high explosive and incendiary substances with consequent disorganization of the transport and essential services. *Mustard gas*

The most likely method of projecting gas on cities is from aircraft, either by bombs or in the form of a spray. Bombs are particularly effective in that they contain a large proportion of filling to total weight and do not tend to bury themselves deeply in the ground on impact. They may be charged with persistent or non-persistent gas, but the gases most likely to be used in this way are mustard gas, lewisite, and one or other of the lung irritants. Tear-gases and arsenical gases are not very harmful but they may be used. Liquid gas carried in tanks by aircraft can be sprayed rapidly over extensive areas, but such a method of release would be effective only against unprotected individuals in the open. For all practical purposes, therefore, defence measures are con- *Method of projecting gas on cities*

cerned with protection against persistent vesicant gases, such as mustard gas, and to a less extent asphyxiant gases.

(2)—Personal Protection

Equipment   For personal protection the most important anti-gas appliance is the respirator. Other anti-gas equipment consists of anti-gas (protective) ointment. Anti-gas (protective) clothing, which is also part of personal protection, is worn only by persons employed on duties in connexion with de-contamination.

Respirators   Respirators made according to Government specifications will give adequate protection against all the true war gases which are likely to be encountered. Carbon monoxide has not been used, nor is it likely to be used, and the respirator does not protect against it. The respirator consists essentially of a container in which are enclosed the purifying agents; a face-piece which is designed to protect the eyes and lungs; and valves, inlet and outlet. The method of attachment of the container to the face-piece varies with the different designs. All the official respirators are constructed on the same principle, and the degree of protection

Filters   afforded is more or less of the same order. The filtering agents consist of two different materials: (i) charcoal to absorb the various gases, and (ii) a filter pad to trap finely divided particles of smoke, such as are produced by the arsenical gases. The charcoal which is used is of a special type and quality and has been selected after considerable research regarding its physical properties. Briefly, the following are the distinctive features of the charcoal which is used. Its fragility is not great; therefore it retains its structure and porosity under conditions of rough usage. It absorbs war gases completely and extremely rapidly and is capable of dealing with large amounts of gas per unit weight. It neutralizes all the true war gases so far used. It is chemically stable and thus can be stored indefinitely without causing any corrosive action on the metal or other parts of the container. The absorptive and adsorptive properties of charcoal, which bring about the neutralization of war gases, depend on its porosity. The more highly porous the charcoal the greater is its value in this respect. It is used in the form of granules; by freeing these granules of volatile hydrocarbons the pores and fissures are enlarged and the absorptive property is increased. This is termed activating the charcoal; activation may be accomplished in various ways. During the War 1914 to 1918 the charcoal was made from coco-nut shells, but more recently charcoal has been prepared from products available in this country.

Effects on the wearer   The main objections to the wearing of the respirator are (i) resistance to breathing, (ii) rebreathing of the residual air confined by the respirator, and (iii) the psychological effect of these factors.

Resistance   The resistance of the container to breathing is expressed in terms of a manometer reading of the pressure required to force a given quantity of air through the container in a given time. Provided this pressure does not exceed a column of four inches of water when three cubic feet of

air are forced through the container in one minute, injurious effects will not be produced by wearing the respirator. The resistance in the official pattern of container is considerably below this figure.

The dead space in the respirator has been reduced to a minimum, so that an insignificant amount of air is rebreathed. *Rebreathing of residual air*

The slight resistance to breathing is liable to be greatly exaggerated by persons of a nervous disposition, who complain of a feeling of suffocation. This, however, is largely subjective and can be overcome by experience and training. *Psychological effect*

Anti-gas (protective) ointment has been advocated provisionally as part of the personal protective equipment. Although this ointment, which is prepared with bleach, will neutralize any liquid mustard gas which has not already penetrated the skin, it will cause irritation if applied often or allowed to remain in contact with the skin for any length of time. This type of ointment cannot be applied to the skin in anticipation of contamination occurring. The use of these ointments as at present prepared is limited to minor degrees of contamination. The application of the ointment to the exposed surfaces only will not prevent the person from becoming a casualty when the clothing has been contaminated. *Ointment*

(3)—Collective Protection

(a) Preparatory Measures

The general scheme suggested is to appoint a Central Gas Defence Directorate which will divide the town into sub-areas self-contained as regards gas defence. Arrangements will be made for the provision of gas-proof rooms in each house as far as possible, common gas-proof shelters in suitable positions, and the sounding of the gas-alarm. Instructions should be issued to ensure that the population is conversant with these measures and knows exactly what to do in the event of a gas-alarm. This knowledge will prevent panic, which is, perhaps, the greatest of all dangers. Special de-contamination squads with protective clothing and the necessary stores and equipment will be organized. During an air raid the police and fire-brigade organizations will be fully occupied with their own special duties.

(b) Treatment of Contaminated Persons and Casualties

All persons who have been contaminated with a vesicant gas will require de-contamination. Casualties may be placed in three main categories, those who require (i) simple de-contamination of the body and of the clothing, (ii) de-contamination together with treatment of the effects of the gas, and (iii) de-contamination together with treatment of gunshot wounds and other injuries. The organization designed to deal with a few casualties is comparatively simple. Difficulties arise, however, when many persons have to be dealt with simultaneously. Plans of a reception station are given in Air Raid Precautions Hand Book No. 1. The accommodation consists essentially of rooms for undressing, wash-

ing, reclothing, and medical treatment. Any scheme formulated should always embody alternative sites. In the evacuation and further treatment of casualties the general scheme is based on that of the Army Medical Service, i.e. certain hospitals will be ear-marked as Casualty Clearing Stations and others as Base Hospitals. There will also be ambulance and auxiliary services.

(c) Protection of De-Contamination Squads

Anti-gas clothing
When mustard gas is encountered the protection given by the respirator alone is not sufficient, since this particular gas affects the skin. In order to protect the skin some form of anti-gas clothing is required. The material advocated at present is a good-quality oilskin fabric, which has the property, when new, of withstanding penetration of liquid mustard gas for a period of approximately four hours. This material can be de-contaminated by boiling, but the protective value diminishes when the fabric has been boiled a few times. A complete anti-gas (protective) suit, which is worn over underclothing, consists of jacket, trousers, hood, and gloves made of oilskin, and rubber gum-boots which extend to the knee. Mustard gas penetrates rubber material, but rubber gum-boots are used because they give a greater period of protection than leather boots, which are difficult, or almost impossible, to de-contaminate. Rubber gum-boots can be de-contaminated by boiling.

Rubber

Oilskin
Oilskin material is non-porous, and the great disadvantage of any kind of impervious fabric, apart from the discomfort of being clothed in such stiff material, is that heat and perspiration from the body are retained inside the suit. There is consequently interference with the normal loss of heat and moisture from the body, which adds to the discomfort of the wearer. If this persists for any length of time, the body temperature rises, the pulse-rate becomes rapid, signs of distress appear, and the condition may eventually develop into complete prostration and collapse. These signs and symptoms are accentuated in warm conditions, the temperature and relative humidity having an important bearing on the length of time the complete suit, together with the respirator, can be worn. No definite time can be laid down, as so many factors are involved, the chief being the atmospheric conditions and the nature of the work. If men are trained and accustomed to work in a respirator and complete oilskin suit, they can as a rule do long spells of manual labour, the period of work varying from half an hour to four hours. The complete oilskin suit should be worn only in circumstances which

Impregnite
necessitate complete protection. Until such times as permeable clothing can be impregnated with compounds such as impregnite, which is capable of neutralizing mustard gas, protection of personnel handling gas casualties must be effected by the use of some modified oilskin covering.

Removal of clothing
Persons employed in a mustard-gas area require cleansing treatment as soon as they come off duty, and they must be given assistance to remove their clothing. Those affording this assistance must in their turn be protected by some form of anti-gas (protective) clothing. When the

protective clothing has been removed, cleansing and provision of fresh underclothing are necessary.

(d) General Considerations

The use of gas has a devastating effect on morale. The explanation of this fact is the ignorance of the people regarding the properties of gas and the lack of simple knowledge of how to avoid its effects, even to appreciating that the safest thing to do during a gas attack is to keep indoors in a closed room at the leeward side of the building.

Undue prominence may at times be given to the development of the offensive side of this type of warfare, but it must be realized that with the introduction of any new agent counter-measures are rapidly brought into being. It may be anticipated, therefore, that some method of protecting the body against the action of the vesicant gases will be evolved.

The proportion of deaths caused by other weapons is infinitely greater *Mortality* than that resulting from the use of chemical agents. The degree of suffering and the period of incapacity following the effects of gas are very *Incapacitation* much less than in the case of gunshot or shell wounds which are much more liable to produce prolonged injury and permanent mutilation.

The use of gas in warfare is forbidden by the Geneva Gas Protocol of 1925, to which this country and all the more important states in western Europe have subscribed. In spite of this agreement, however, the likelihood of gas being used is very great, since it is only reasonable to assume that when a nation is fighting for its existence the temptation to use such a powerful weapon is unlikely to be resisted. Further, the agents suitable for chemical warfare are either products that are in everyday use or allied compounds readily prepared with the plant available in any well-developed chemical industry.

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GASTRIC ULCER

See PEPTIC ULCER

GASTRITIS

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Reference may also be made to the following titles:

ACHLORHYDRIA HAEMATEMESIS

ANAEMIA HYPERCHLORHYDRIA

DYSPEPSIA PEPTIC ULCER

STOMACH DISEASES

1.—DEFINITION

(Synonym. —Gastric catarrh)

558.] In the past the name gastritis has been widely applied to disorders of gastric function without reference to exact symptomatology or pathology. Indeed it was impossible to establish the pathology of the condition or to determine how often gastric symptoms were associated with organic changes. At the beginning of this century the development of methods of precision in gastric diagnosis by means of improved operative methods, radiology, and fractional test-meals led to the better understanding of peptic ulcer and cancer and to a closer study of the symptoms they produce, but gastritis eluded recognition, and, when a definite lesion could not be demonstrated, it came to be thought that gastric symptoms were of reflex or nervous origin, and for a time the term 'nervous dyspepsia' almost took the place of 'chronic gastritis'. The pendulum is now swinging back, as means of examining the inside of the stomach with the gastroscope during life have been evolved, and methods of histological study of the tissues in an absolutely fresh state are being perfected. Animal experiments have also contributed greatly to knowledge of the subject. It is now recognized that gastritis is astonishingly common, existing sometimes with and sometimes without symptoms, and associated sometimes with ulcer, cancer, anaemia, or achlorhydria. That the first International Congress of Gastro-enterology in 1935 chose the subject of gastritis for discussion shows what an important place it now occupies. A wide field of investigation is opening up, and it will probably be many years before the chapter on gastritis can be written in full.

2.—AETIOLOGY

The recognition of gastritis as a definite morbid change in the living subject and in tissues removed from the body is still difficult. Much of the older work based on the examination of post-mortem material is useless, as changes occur within fifteen minutes of death. The true incidence and aetiology of the disease are therefore incompletely known.

Two main aetiological groups are recognized: (1) haematogenous gastritis caused by blood-borne toxins; and (2) irritation gastritis caused by substances taken directly into the stomach.

(1)—Haematogenous Gastritis

This is probably of great importance and much commoner than is recognized clinically. Many of the infections known to be potential causes are common, e.g. diphtheria, pneumonia, influenza, measles, enteric, syphilis, severe burns, and pyogenic infections, especially with

streptococci. Metabolic toxins, as in uraemia, may act directly on the stomach or, by lowering resistance, prepare the soil for bacterial infections. Examples of this type of gastritis may be given. Faber found that in a child who died on the third day of acute diphtheria the whole mucous membrane of the stomach was oedematous and hyperaemic with blood extravasations and an enormous infiltration of polymorphonuclear leucocytes; areas occupied by superficial haemorrhages had become necrosed and formed erosions in many places. Vimtrup reported the case of a young man who died of influenza and had an acute gastritis with erosions involving the whole organ from cardia to pylorus, a condition of 'pan-gastritis'; except for vomiting there had not been any sign of the condition during life. In dogs with an artificial gastric fistula similar inflammatory changes have been produced by the injection of diphtheria toxin (E. Thomsen).

The rare condition known as phlegmonous gastritis belongs to the *Phlegmonous gastritis* group of cases of haematogenous origin; it is associated with acute general infections, but the lesion is not caused by the toxins only; nor is it limited to the mucosa and submucosa; the whole gastric wall is involved, and the infecting organism is found in the tissues. Intense hyperaemia, oedema, and polymorphonuclear infiltration are present, and there is purulent infiltration of the submucosa, which on incision exudes beads of pus. The entire stomach may be involved, but circumscribed forms are also described. Streptococcal infections are said to have been present in 70 per cent of cases; staphylococcal, *B. coli*, and pneumococcal infections are also reported.

(2)—Irritation Gastritis

This is produced by the ingestion of irritating substances or poisons which act directly on the mucosa; the action may be chemical or physical. Of substances commonly taken alcohol in excess is one of the most powerful irritants. Coarse food also may produce irritation gastritis, as shown experimentally in young calves fed on a rough diet (Simpson). Substances producing 'food-poisoning' may affect the mucosa directly or by a toxic action after absorption. On similar diets containing irritating substances some persons develop gastritis and others escape; a second factor, such as idiosyncrasy, must be necessary for its development. One of these determining factors is a hyperchlorhydria which appears to be a constitutional and persistent condition. This effect of *Effect of hyperacidity* hyperchlorhydria has been confirmed experimentally in guinea-pigs. The animals' stomachs were kept hyperacid for a long period and they were then given minute amounts of mustard oil. The experimental animals developed gastritis, and the control animals on the same doses were unaffected.

(3)—Gastritis due to Defective Diet

The general character of the diet is probably of great importance in the aetiology of gastritis, in respect of the balance of foodstuffs, protein,

fat, and carbohydrate, of adequate mineral and vitamin content, and of the physical state in which it is taken. The vitamins may indeed have a specific effect on the gastric mucosa, for vitamin A is considered to promote the resistance of epithelial tissues to infection, and the vitamin B complex is concerned in the causation and cure of one form of the macrocytic anaemias, which are closely linked with achlorhydria and gastritis. Experiments on dogs with diets deficient in vitamin B showed that gastric acidity might be diminished or abolished by this deficiency (Cowgill and Gilman).

3.–MORBID ANATOMY AND PATHOLOGY

Macroscopic appearances　　The mucous membrane studied by the gastroscope presents very varied appearances, as acute and chronic gastritis may both be present at the same time. Oedema is often accompanied by congestion, haemorrhages, and erosions, which may be punctiform or linear, large or small. The gastritis may be generalized or occur in patches. The swelling may involve the epithelial structures or the submucosa or both. The affected mucous membrane is very easily injured, and the changes are therefore more pronounced along prominent rugae or where there is a localized rigidity due to muscle spasm or scar tissue. Gastritis may lead either to hypertrophy with hyperplasia or to atrophy. Hyperplasia may be extreme and a polypoid condition develop. Atrophy may occur in patches and is recognized by the obliteration of the mucous folds and the visibility of the network of vessels. Mucosal structures may be diminished to a fraction of their normal thickness, and the submucosa, which is normally very soft and supple, may become rigid as the result of fibrosis.

Microscopic appearances　　Microscopic examination confirms these findings. Many minute erosions develop apparently as the result of desquamation or as a sequel to small haemorrhages and necrosis. Oedema and polymorphonuclear infiltration are present. Lymphoid cells may be increased, especially in the region of the pylorus—a condition which is sometimes called chronic follicular gastritis.

4.–ASSOCIATED PATHOLOGICAL CONDITIONS

Peptic ulcer　　Gastritis and peptic ulcer are often present in the same stomach, but the nature of the association is not determined. Some authorities consider that gastritis with erosions precedes the formation of the chronic penetrating ulcer, and that chronic ulcer develops at the site of an erosion; others hold that chronic ulcer is not the sequel of an erosion but arises quite independently and has a different causation. It is possible that peptic ulcer may arise in either of the above ways, and this view is held by Moutier.

Gastritis is always present in cancer of the stomach. Achlorhydria is *Cancer* found in 75 per cent of cancer cases, and in some persons gastritis has been known to be present for years (thirty years in a case reported by Faber) before cancer developed. Cancer may follow polypoid hyperplasia, which is a sequel of gastritis. Not all cases of gastritis with achlorhydria develop cancer; a second factor must be essential, perhaps an hereditary or constitutional predisposition. Cancer may also develop at the site of peptic ulcer, in which case an associated gastritis is always found, but an acid secretion is present.

Syphilis of the gastric mucosa has been considered until recently to be *Syphilis* rare, but as precise diagnosis can now be made with the gastroscope a further study of the subject will reveal how often it really occurs. Formerly 'syphilitic catarrh of the stomach' was occasionally diagnosed when symptoms of dyspepsia were present with low or absent gastric acid in a syphilitic subject. Bonadies reported that gastroscopic examinations showed gastritis to be not uncommonly present together with active syphilis. That the infection is the specific cause of the condition has not been proved, and the gastroscopic appearances do not present any diagnostic characteristics but are extremely varied. Hypertrophic or atrophic gastritis may be seen or a simple mucous catarrh. Antisyphilitic treatment is usually accompanied by relief of symptoms, but Bonadies found that, as in other forms of gastritis, the local condition of the stomach did not necessarily show a parallel improvement.

5.–EFFECT OF GASTRITIS ON GASTRIC SECRETION

Gastritis is found both experimentally and in human subjects to cause *Acid* a partial or complete suppression of the acid secretion. It has been shown above that infective diseases may cause severe gastritis without definite symptoms. Bloch, who studied the effect of infective disease on the gastric secretion of infants, found that a lowering or suppression of acid *Suppression* occurred temporarily in 50 per cent of children observed. This suggests *of secretion* how commonly gastritis may occur in the child population, for there is no evidence that achlorhydria is produced by any disease other than that of the gastric mucosa (Simpson). Repeated attacks of gastritis during acute infections may lead gradually, at least in susceptible individuals, to the achlorhydria which becomes commoner with advancing years.

Histologically the cause of the achlorhydria is severe damage to the *Histology* oxyntic or acid-forming cells, which appear in some cases to be specifically affected, and although regeneration of glandular elements may take place these lack the specific acid-forming function. Histologically a distinction can be drawn between two forms of achlorhydria which correspond to the clinical types. In one the oxyntic cells appear to be extensively atrophied. This form, which does not respond to treatment, is found in pernicious anaemia. In the other form the cells appear fairly

normal, although a superficial gastritis with much mucous secretion is present. This form is associated with an irritation gastritis, and the active secretion may be restored by the withdrawal of the irritant and by appropriate treatment (see ACHLORHYDRIA, Vol. I, p. 126).

Peptic ulcers   When gastritis is present together with peptic ulcer, a condition associated with constitutional hyperacidity, the tendency to depression of the acid function is masked by the original hyperacidity; so what appears to be a normal acid-curve may be obtained with the fractional test-meal. With treatment and healing of the ulcer the gastritis is also improved, and the hyperacidity is again manifest when the test-meal is repeated.

Pepsin   The secretion of pepsin has not been studied so fully as that of hydrochloric acid; it is not so readily affected by gastritis, but is low or absent in pernicious anaemia.

6.–ENDOCRINE SECRETIONS AND GASTRITIS

The injection of pituitary (posterior lobe) extract in animals produced a striking effect on the gastric mucosa (Dodds and Noble). In a large dose it caused a necrosis of the area of the oxyntic cells and in smaller repeated doses the development of a solitary ulcer resembling peptic ulcer in man. Other experiments have shown that the vasopressor fraction of posterior pituitary extract caused complete suppression of gastric secretion and abolition of the response to histamine, producing a temporary condition of achlorhydria (Dodds and Noble, 1937).

7.–CLINICAL PICTURE AND SYMPTOMS

(1)—Acute Haematogenous Gastritis

(a) Haematogenous Toxic Gastritis
The chief symptoms are usually those of the primary condition, e.g. influenza, diphtheria, or scarlet fever, with which loss of appetite, nausea, and vomiting are commonly associated; but the degree of true organic gastritis accompanying these symptoms in any individual case is unknown. Sometimes the evidence of true gastritis is unmistakable; the vomiting is persistent and contains an admixture of blood in small amounts, such as arises from a congested or eroded mucous membrane, and epigastric pain and tenderness are present.

(b) Phlegmonous Gastritis
This very rare condition usually follows some infection such as pneumonia but may develop suddenly without any indication of the primary infection. The onset is with epigastric pain and vomiting, both, usually but not always, acute and persistent. In the acute type the patient is restless and anxious and becomes collapsed, the clinical aspect being

that of an upper abdominal emergency. The usually copious vomit contains mucus and blood; a remarkable appearance of the vomit as of bright red jelly has been described (Jennings Marshall). The difficulty of diagnosis is insisted on in the reported cases.

(2)—Acute Irritation Gastritis

The symptoms of gastritis due to inorganic poisons and to food poisoning, alcohol, and the like vary with the nature of the irritant, the relative degree of local action on the stomach and intestines, and of toxic action after absorption. There are more or less epigastric pain, tenderness, and vomiting; at first the stomach contents are vomited, later fluid secretions, mucus, blood, and bile. Persistent hiccup may occur and makes the prognosis serious.

(3)—Chronic Irritation Gastritis

This type of gastritis gives rise to many symptoms, usually associated with the taking of food, especially when this is of an irritative or indigestible character. It leads to loss of appetite or voluntary restriction of intake and to a vicious circle of malnutrition and aggravation of symptoms. The symptoms are often irregular in their incidence from day to day, varying with the physical and mental condition of the patient; but there are also long periods of exacerbation and remission such as occur in peptic ulcer patients. The chief complaints are of epigastric pain or discomfort, eructations often due to aerophagy, heartburn, nausea, and vomiting. Recent workers have put forward the opinion *'Ulcer pains'* that periodic pains of well-defined character, which are called 'ulcer pains' and have been said to be pathognomonic of ulcer, are due, in fact, to an active gastritis, present sometimes with and sometimes without an ulcer. This point needs further investigation. If 'ulcer pains' are actually due to gastritis, this would explain the cases in which typical pains are present but no ulcer can be demonstrated either by X-rays or at operation.

Profuse haematemesis may arise from gastric erosion and cause an *Profuse* alarming or fatal loss of blood. The patient usually survives the first *haemat-emesis* haemorrhage, but a recurrence within a few hours or days is generally fatal. Gastric pain is usually absent. There may be a tendency to recurrent attacks. Scheiner gave an account of a young man of thirty, who, otherwise healthy, had several attacks of haemorrhage, thought to be pulmonary, over a period of four years. By gastroscopy an erosion of the stomach was found on the lesser curvature and during treatment was seen to heal. Eight months later he returned with an acute generalized gastritis.

Some forms of chronic gastritis do not give rise to symptoms. If the *Chronic* presence of achlorhydria is admitted as evidence of chronic gastritis or *gastritis without* of an atrophic condition of the glands which has followed an acute *symptoms* attack, this type of gastritis may certainly be unaccompanied by symptoms, for it may be found in healthy young adults who have never

had any dyspeptic symptoms and do not give any history of illness resembling an acute attack of gastritis (Bennett and Ryle).

8.–DIAGNOSIS

(1)—Acute Gastritis

Acute gastritis associated with infections is often unrecognized, for symptoms pointing to special involvement of the stomach may be completely absent, but the presence of vomiting will suggest gastritis, and blood in the vomit will establish the diagnosis.

Acute gastritis associated with the taking of a powerful irritant may be diagnosed from the history and the rapid development of the symptoms —-vomiting, epigastric pain, and collapse. Blood often occurs in the vomit if this is severe. The material first vomited should be kept for examination, especially if there is any doubt about the cause of the attack, for the vomit may afford the chief evidence in cases of accidental, suicidal, or criminal poisoning.

Phlegmonous gastritis is admittedly very difficult to diagnose, as the clinical symptoms are so variable; moreover, the condition being very rare, the possibility of its occurrence is forgotten.

(2)—Chronic Gastritis

The differential diagnosis of chronic gastritis and its causes is among the most important and most difficult duties of the medical practitioner. The list of causes or associated conditions is formidable, yet these must be constantly borne in mind whenever a patient with 'indigestion' presents himself for diagnosis and treatment. The symptoms resembling simple 'indigestion' may arise with cancer; ulcer; chronic infections such as pulmonary tuberculosis and syphilis; chronic abdominal infections such as cholecystitis, appendicitis, and salpingitis; acute and chronic anaemia, either primary or secondary; heart disease with congestive failure; and vascular and renal disease, acute and chronic. It is not known how often the gastric symptoms which arise in the course of these diseases are, in fact, due to organic gastritis; but, as the treatment is mainly that of the primary condition, the importance of giving close attention to accurate diagnosis cannot be over-emphasized.

Causes of 'indigestion'

The routine diagnostic procedure must include a full history of symptoms going back to early life and an inquiry as to occupation, diet, meal-times, and habits as regards mastication, alcohol, tea, coffee, and tobacco. An account of the home life and conditions and of mental, nervous, and occupational strains may reveal important diagnostic points.

Clinical history in diagnosis

The complete physical examination must include the lungs, heart, and kidney functions, the routine examination of the whole of the gastro-intestinal tract from the buccal mucous membrane, tongue, tonsils, and teeth, to the rectum, as well as careful examination of the abdomen and

Physical examination

pelvis. Before the palpation of the abdomen the patient should be asked to point out the actual site and distribution of the pain, and inspection of the abdomen for alteration in the contours or visible peristalsis should precede palpation.

It will probably be a long time before the early diagnosis of gastric *Cancer and* carcinoma is the rule and not the exception. It arises in the presence of *gastritis* chronic gastritis and, if the growth does not cause any mechanical obstruction, there may be little to attract the attention of doctor or patient to the serious character of the condition. Dyspeptic symptoms which come on for the first time in middle age and for which no immediate cause can be found require the fullest investigation. If careful examination, simple tests, and treatment for a short period of three or four weeks do not provide a diagnosis or cure, the patient must at all costs be referred to a hospital or other diagnostic centre for full examination. If the results lead to even a suspicion of cancer, an exploratory operation is well justified; delay till the diagnosis is beyond doubt usually allows the favourable moment for radical cure to pass.

In all conditions calling for full differential diagnosis test-meals, X-ray *Diagnostic* examinations, blood examination, Wassermann reaction, and, if avail- *investigations* able, gastroscopic examination must be used.

In chronic gastritis a fractional meal usually shows great excess of *The fractional* mucus with pus and low or absent acid secretion and rapid emptying. *meal* This response is found in cancer, in chronic irritation gastritis, and in chronic hypochromic microcytic anaemia. Injection of histamine acid phosphate gives a more complete test for the degree of acid secretion.

The diagnosis of gastritis and the study of the mucosa are made *X-ray* radiologically by a special technique to show the pattern, depth, width, *examination* and irregularities of the rugae. This technique is very specialized, and its value to clinical diagnosis is not yet generally acknowledged. Radiology is chiefly used for the differential diagnosis of cancer and ulcer from chronic gastritis.

The gastroscope offers an important new method of diagnosis (see *Gastroscopy* ENDOSCOPY OF THE UPPER RESPIRATORY AND ALIMENTARY TRACTS, p. 17). It has been used for some years by a few specialists, but the invention of a flexible gastroscope within the last few years has led to greater safety and more useful results. The instrument should be used only by those who have made a special study of the technique and are aware of its dangers. The appearances have been mentioned above (p. 536). The gastroscope provides a great advance in differential diagnosis, in the early detection of cancer, and in the diagnosis of those forms of chronic gastritis without dyspeptic symptoms which are associated with the anaemias.

The diagnosis of a syphilitic gastritis is based on the finding of a *The Wasser-* positive Wassermann reaction. There are not any special distinguish- *mann reaction* ing clinical symptoms, and chemical, radiological, and gastroscopic investigations do not show any special features.

9.—TREATMENT

The symptoms may disappear with remarkable rapidity under treatment, whereas the lesions persist with tenacity for many weeks and heal slowly. The tendency to recurrence on slight provocation remains for years. *Relief of symptoms must not be interpreted as cure of the disease.*

The chief maxims to be remembered are: (i) treatment must be continuous and prolonged; (ii) the diet is of first importance; (iii) physical and mental rest, complete or partial, promote healing; (iv) avoidance of fatigue and freedom from worry help to prevent relapse; (v) drugs are in general palliative and not curative; and (vi) the gravity of the diseases which follow gastritis makes treatment of the early stages of major importance.

(1)—Acute Gastritis

Diet

In the first 24 to 48 hours all food may be withheld and water alone given in small amounts of 3 to 4 ounces. If it is certain that there is not present any intra-abdominal complication causing the vomiting and epigastric pain, morphine may be given. If water is not retained by the stomach, glucose-saline injections may be given per rectum. When the acute symptoms are past, fluid foods such as milk are given. Whole milk is not always well tolerated, chiefly on account of the fat. Separated milk with the addition of sodium citrate, 1 grain to each fluid ounce, is more easily digested; it may be slightly flavoured with tea, coffee, or chocolate. Dried milk preparations are useful. Raw eggs and raw egg-albumen are not so digestible as lightly cooked eggs, which may soon be added. 'Thickened feeds', such as thin gruel or patent invalid foods, may be used. Sugar, if tolerated, supplies energy in concentrated form, is readily absorbed, and helps to tide over a crisis when it is necessary to feed the patient while giving the minimum amount of work to the stomach; 4 ounces of sugar (120 grams) daily supply about 500 calories or nearly half the average requirements of an adult at complete rest.

Gastric lavage

Lavage may check continuous vomiting, but it is not wise to pass a tube if there is blood in the vomit or some acute irritant has been swallowed. If the patient is able to co-operate, the washing out may be done by giving several glasses of lukewarm water or sodium bicarbonate in physiological saline (a teaspoonful to the pint). The first two or three glasses will probably be vomited and the irritating contents of the stomach washed out or diluted, after which the fluid may be retained in the stomach. After the acute phase is over it is well to err on the side of caution and to continue a bland diet after all digestive symptoms have disappeared for at least a week or more according to the nature of the attack.

Vitamin content of the diet

All diets given for a period of more than a week or ten days must be scrutinized with reference to their vitamin content and, if necessary, supplemented with vitamin concentrates. Citrus fruit juices containing

vitamin C are usually easily taken. A yeast product, such as marmite, may be given to supply vitamin B, and halibut-liver oil in capsules supplies a concentrated form of vitamins A and D.

(2)—Chronic Gastritis

The general principles of treatment are similar to those now adopted for the treatment of chronic peptic ulcer. When symptoms are active the patient is confined to bed; if possible this should be for not less than a fortnight or three weeks. Small meals of bland easily digested food are *Frequent* given at intervals of two hours, and this regime is maintained for the *small feeds* full period. If the patient is unable to leave work a compromise must be made in the diet treatment, but the same principles of small meals at short intervals should be adhered to.

It is extraordinary how often indigestion is 'treated' without any *Errors in* attempt to regulate the meal times and arrangement of the diet, although *treatment* such dietetic errors often cause or aggravate the trouble. There may be long hours of work after a breakfast of tea and a biscuit, perhaps a scanty lunch, and then a large solid meal after work, when the stomach, together with the rest of the body, is exhausted and the food, although badly needed, cannot be digested. A re-arrangement of meal times and diet will do far more than drugs to remedy the trouble. Again, many chronic dyspeptic women take an incredibly small and limited diet and believe that they are unable to eat more. A period of rest in bed with small frequent feeds may be necessary to break this habit of semi-starvation and by building up the general nutrition will gradually restore the normal gastric functions. (See also ANOREXIA NERVOSA, Vol. I, p. 598.)

The importance of a maintenance diet adequate in first-class protein *The mainten-* and good fats, with fresh salads and fruits or fruit juices, and not con- *ance diet in* taining too high a proportion of starchy foods must be remembered, *and after* and the patient must be advised accordingly; the tendency to take a preponderantly starch diet, almost vitamin- and iron-free, is hard to eradicate. Each meal, however light, should contain in addition to bread or biscuit some foodstuff such as egg, cheese, fish, milk, or fruit. Foods containing coarse residues ('roughage') with fibres, skins, pips, and indigestible cellulose must be excluded. If long fasting cannot be avoided occasionally or if the patient is fatigued and hungry, a *very* small light meal should be eaten, and when the patient is rested the appetite can be satisfied more completely. A large meal eaten when the patient is fatigued is almost certain to cause a relapse. The food must at all times be well prepared and properly masticated with good teeth.

For many months the patient must avoid alcohol, mustard, pepper, *Abstention* vinegar, spices, and other irritants. Weak tea and coffee only are allowed. *from irritants* Tobacco is a definite irritant, and smoking should be allowed only in the strictest moderation and never on an empty stomach.

The alkaline salts greatly relieve symptoms: sodium bicarbonate and *Drugs* the carbonates of bismuth, magnesium, and calcium are most frequently

used and are given in rather large doses; they have a sedative rather than a curative effect; opinions about their mode of action differ.

Iron in the treatment of gastritis

Iron is valuable in all cases with anaemia, and in patients with hypo-chromic microcytic anaemia with achlorhydria it is absolutely essential. Patients and their doctors often believe that the iron causes indigestion, and it is therefore given up after a short trial, but this discomfort is usually transitory, and the iron should be continued. Iron by injection is useless. The preparations of iron most easily taken are the iron and ammonium citrate in doses of 20 to 30 grains (1·2 to 2·0 grams) three times a day or Blaud's pill in similar doses. The latter preparation may be obtained in capsules containing 25 grains and is more certain of absorption in this form than as a pill.

Hydrochloric acid

The use of acid in gastritis with achlorhydria is advocated (for details of administration see ACHLORHYDRIA, Vol. I, p. 126).

Gastric lavage

Lavage is a valuable form of treatment for gastritis with excessive mucous secretion and achlorhydria. Solution of hydrogen peroxide (about one fluid drachm to the pint) is used at first and the strength gradually increased. The gastritis is definitely improved, and the secretion may be restored by this treatment. (For full description of the methods see ACHLORHYDRIA, Vol. I, p. 130.)

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GASTROPTOSIS

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See NEUROSYPHILIS

GENU RECURVATUM, VALGUM AND VARUM

See JOINTS, DISEASES AND DISORDERS

GERMAN MEASLES

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Reference may also be made to the following titles:

GLANDULAR FEVER   MEASLES
SCARLET FEVER

1.–DEFINITION

(Synonyms.—Rubella; epidemic roseola)

559.] German measles is a specific infective eruptive fever with no relation to measles or scarlet fever, breeding true, and protecting only against itself.

2.–AETIOLOGY

German measles, occurring less commonly than measles, appears in *Incidence* epidemic waves, most often in spring and early summer. The age incidence is higher than that of measles, children under five being seldom affected. Its frequency diminishes after the age of thirty. The sexes are affected equally.

Infectivity   The infectivity is less than that of measles and is highest during the prodromal and early eruptive stages. Infection is spread by catarrhal discharges from the nose and throat, and there is not any evidence that it ever spreads by fomites or by a third person.

3.—CLINICAL PICTURE

Incubation and quarantine   The usual period from exposure to the appearance of the rash is eighteen days, and the extreme limits are from nine to twenty-one days. The quarantine period advised by the Medical Officers of Schools Association is twenty-one days.

(1)—Premonitory Symptoms

Onset   The rash is often the first symptom noticed, especially in children. If premonitory symptoms occur they are usually mild and begin 24 to 36 hours before the rash appears. They may consist of headache, coryza, slight sore-throat, and an ill-defined feeling of illness. Vomiting is rare, but frequently the suboccipital, mastoid, and cervical glands are swollen two or three days or even a week before the eruption begins, and the patient may complain of a stiff neck.

(2)—Symptoms of Eruptive Stage

The rash   The rash usually appears first on the face, on the temples at the roots of the hair, or behind the ears. It is made up of pale pink discrete spots, smaller than those of measles and less raised. It spreads rapidly over the face, including the circumoral region, and over the trunk and limbs. The dorsum of the foot is usually the last region to be affected. It is rare for the rash to be equally intense all over the body. At first the spots tend to cluster into small groups, but sometimes when the eruption becomes more profuse they coalesce and produce a scarlatiniform appearance. By the time this has happened on the trunk, the rash on the face has usually begun to fade, leaving the circumoral ring clear, and the resemblance to scarlet fever may be very striking.

The average duration of the eruptive stage is from 24 to 36 hours, but it may be as short as 12 hours or last as long as four days. No definite staining of the skin follows and, although sometimes there may be a little branny desquamation of the face, there is not any real peeling.

Two varieties   Many school doctors recognize two distinct types of rash, a discrete circular macular and a scarlatiniform, and consider the macular to be less infective than the scarlatiniform.

Concomitant symptoms   During the eruptive stage there is usually some catarrh with a little sneezing, coughing, and conjunctival injection. There is, however, no lacrimation, photophobia, or persistent cough as there is in measles. There may be slight sore-throat owing to congestion of the fauces and soft palate, but the buccal mucous membrane is generally unaltered.

Temperature   In children and in most adults the temperature is only slightly raised,

if at all, and is not as high, nor does the patient feel so ill as the amount of rash would seem to warrant. In some adults, however, it may reach 102° F. or higher, and the constitutional disturbance may be considerable.

If the lymphatic glands have not become enlarged during the prodromal *Glands* stage, they become so during the stage of eruption. The suboccipital glands are those most constantly affected and may be as large as filberts. Those lying along the posterior border of the sternomastoid can be felt as firm discrete, pea-like, freely movable masses, and the epitrochlear, submandibular (submaxillary), and inguinal glands may be easily palpable. They never suppurate, and subside quickly as a rule. Exceptionally the swelling may persist for several weeks, and in rare cases some enlargement may be permanent. Convalescence is usually rapid.

4.–COMPLICATIONS

Complications are almost unknown in Great Britain. Transient albuminuria, slight bronchial catarrh, and rheumatic pains are said to occur occasionally. In Continental and American literature, however, many reports of serious complications may be found. Meningo-encephalitis, meningo-myelitis, polyarthritis, and isolated cases of Landry's paralysis, streptococcal septicaemia, and purpura haemorrhagica have been recorded. The evidence is not very conclusive that in some of these cases at any rate the primary disease was really German measles.

It has often been noticed that German measles and acute catarrhal *'Pink eye'* conjunctivitis of the variety known in schools as 'pink eye' are prevalent at the same time. Dukes went so far as to think that 'pink eye' might be the only sign of the disease. Whether this association is real or accidental is uncertain.

5.–DIFFERENTIAL DIAGNOSIS

Diagnosis can be very difficult, especially in isolated cases at the beginning of an epidemic or when other exanthemata are prevalent at the same time. The figures given by J. D. Rolleston of admissions to the London Metropolitan Asylums Board Hospitals show the frequency of mistakes. The divergent statements of patients who claim to have had multiple attacks of measles or German measles and of experienced *Multiple* physicians who seldom if ever see second attacks can be explained only *attacks* in this way.

Infectious diseases which may simulate German measles are measles, *Differential* scarlet fever, and glandular fever. Other conditions likely to cause *diagnosis* mistakes are erythema scarlatiniforme, pityriasis rosea, and syphilitic roseola. Rashes due to drugs, articles of diet, enemas, and injection of antitoxic serum may sometimes simulate German measles.

Two diseases, exanthema subitum and erythema infectiosum, long recognized and often described abroad, have attracted little attention in this country. It may be that they account for some of the so-called multiple attacks of German measles.

Exanthema subitum was described by Zahorsky in 1910 and since then by Glanzmann, Fischof, Ryden, Willi, and others. It usually attacks infants under the age of two years. In a typical case an average of three days' fever precedes the eruption, the appearance of which coincides with a fall of temperature. The rash may closely resemble that of German measles, and confusion is most likely to arise if the feverish stage is mild and its symptoms are unnoticed. Slight sore-throat and some enlargement of the cervical glands may be present, but the general glandular enlargement of German measles is absent. Leucopenia is present with relative lymphocytosis.

Erythema infectiosum is an epidemic disease which has been described by Lozano, Zikowsky, Lind, and others and is sometimes called the fifth disease. Some days of ill health and sore-throat usually precede the eruption, which begins on the cheeks as a butterfly-shaped area of skin which becomes hot and tender. The rash spreads slowly at the periphery and fades in the centre, invading the lateral aspects of the limbs in large round erythematous patches, which may last for several days or even a fortnight. The blood picture is variable, and eosinophilia and lymphocytosis have both been described.

The diseases most likely to be confused with German measles are measles, scarlet fever, and glandular fever. In favour of German measles the most important points are a paucity of prodromal symptoms, a small amount of constitutional disturbance, general glandular enlargement, and a dimorphic rash.

In favour of measles are marked prodromal catarrhal symptoms with a frequent dry cough, some constitutional disturbance with high fever, bronchitis, and the condition of the mouth and throat. During the prodromal stage the soft palate often presents a speckled appearance, which is in well-marked contrast with the uniform congestion of German measles and the vivid colour of scarlet fever. Koplik's spots if present are pathognomonic. Glandular enlargement is not a prominent feature; the cervical rather than the occipital glands are most affected. The rash is bluer and less pink than that of German measles, lasts longer, and stains the skin.

In favour of scarlet fever are the abrupt onset, with headache, vomiting, and sore-throat, and the short prodromal period. The fever is high and the pulse more rapid than the temperature warrants. The soft palate and fauces are vividly and uniformly injected. If adenitis is present, the tonsillar rather than the occipital glands are affected. The rash is punctate and erythematous and spares the circumoral region. The edges are less likely to be morbilliform than in German measles. In later stages glandular suppuration, arthritis, nephritis, or peeling will clinch the diagnosis.

The following table of classified symptoms is a slight modification of that compiled by Dawson Williams:

	GERMAN MEASLES	MEASLES	SCARLET FEVER
INCUBATION PERIOD	9 to 21 days—usually 18.	7 to 14 days—usually 10 (14 days to rash).	1 to 8 days—usually about 2.
PRODROMAL SYMPTOMS	Short and slight.	3 to 4 days. Generally marked.	A few hours. Vomiting common.
RASH	First or second day. Commonly first symptom—rosy red macular, first on face or at roots of hair.	Fourth day. Bluish red papular, first on face or behind ears.	Second day. Brick red. Skin burning.
MOUTH AND THROAT	Slight diffuse injection of fauces and soft palate. Buccal mucous membrane unaltered. Koplik's spots absent.	Prodromal red patches on soft palate and buccal mucous membrane. Koplik's spots present.	Throat affection proportionate to skin eruption. Fauces and soft palate dusky red with exudate on tonsils. Koplik's spots absent.
CATARRHAL SYMPTOMS	Nasopharyngeal catarrh slight. Conjunctivae suffused. Bronchitis uncommon.	Sneezing and frequent dry cough. Lacrimation and photophobia. Bronchitis.	Conjunctivae and bronchi unaffected.
LYMPHATIC GLANDS	Generally enlarged, particularly suboccipital, posterior cervical, epitrochlear, and inguinal.	Enlargement not marked early.	Submandibular and cervical glands chiefly affected.
GENERAL SYMPTOMS	Little or no depression. Tongue clean or slight fur. Appetite often retained. Temperature may be normal. Pulse little altered or accelerated in proportion to fever.	Depression generally marked; often with prostration. Tongue furred. Little or no appetite. Temperature rises gradually to 103° or 104° F. at height of rash. Pulse generally accelerated in proportion to fever.	With much rash, much depression. Tongue coated, peeling on 4th day leaving 'strawberry' tongue. Temperature always raised. Pulse always accelerated, commonly out of proportion to fever.
CONVALESCENCE	Rapid.	Commonly more protracted.	Often prolonged owing to complications.

In glandular fever a maculopapular eruption sometimes occurs and in conjunction with glandular enlargement may suggest German measles; but in glandular fever adenitis usually begins later than in German measles (on the second to the fourth day) and the glands behind the middle of the sternomastoid are those most affected. The eruption occurs later than in German measles. *From glandular fever*

Pityriasis rosea usually begins with a single herald patch on the trunk or neck, with a pink margin and a yellow scaly centre. Gradually after an interval similar patches appear elsewhere and may cover most of the *From pityriasis rosea*

trunk. There is no adenitis and no catarrh, and the eruption usually lasts six weeks.

From syphilitic roseola

In syphilitic roseola a primary sore is present with shotty adjacent glands, which, together with the appearance of the throat and the distribution of the eruption, which in this disease usually spares the face, should establish the diagnosis. In doubtful cases the Wassermann reaction should be tested.

From rashes due to drugs or diet

Rashes due to drugs, articles of diet, enemas, and the injection of antitoxic serum are usually mainly urticarial. The history may give the clue to the diagnosis.

Blood examination

Examination of the blood may be of some help in doubtful cases.

In German measles leucocytes resembling plasma cells are present, with eccentric nuclei and vacuolated intensely basophil protoplasm. They occur during the prodromal stage but become most numerous between the third and sixth days after the eruption. These cells are said to be never present in scarlet fever, measles, or erythema infectiosum (Brusa).

Measles is accompanied by leucocytosis affecting the neutrophils during the eruptive stage, followed by leucopenia when the eruption has faded (Rolleston).

In scarlet fever there is leucocytosis chiefly affecting the polymorphonuclear cells.

In glandular fever there is lymphocytosis (Tidy; Brusa).

In exanthema subitum there is leucopenia with 80 to 90 per cent of lymphocytes (von Bókay; Braunstein).

'Fourth disease'

The existence of the 'fourth disease' described by Clement Dukes of Rugby in 1900 is not now generally accepted; but there is no doubt that different epidemics of German measles, like different epidemics of influenza, vary considerably in detail. In some the rash is inclined to be more scarlatiniform than in others, and some produce more pronounced glandular enlargement. Presumably all these are variations of one and the same disease, but so experienced an authority as Claude Ker admitted that 'we are occasionally confronted with rashes which quite defy classification'.

6.–PROPHYLAXIS

As the infectivity of the disease is probably at its height during the pre-eruptive stage and prodromal symptoms are often absent, it is clearly impossible to be certain of cutting short an epidemic unless all susceptible contacts are isolated. This is a considerable undertaking with a disease the incubation period of which may be as long as twenty-one days, although isolation of contacts from the tenth to the twenty-first day offers some chance of success. Even this may be considered of doubtful advantage in so trivial a malady. The palpation of the glands of contacts and the recognition of the importance of a complaint of stiff neck will enable many cases to be detected in an early stage. Trans-

mission is by direct contact with a patient or with articles freshly contaminated by nasopharyngeal discharges. The infection is very short-lived, and terminal disinfection other than ordinary cleaning and airing is unnecessary.

7.–TREATMENT

Treatment is entirely symptomatic. In many cases it is not required, but if there is any fever the patient should remain in bed on a light diet until the temperature has fallen. The period of isolation need not be more than seven days, according to the advice of the Medical Officers of Schools Association, provided that catarrhal and other symptoms have ceased. In all probability the period is unnecessarily long.

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GIARDIASIS

GIDDINESS

VON GIERKE'S DISEASE

GIGANTISM

GLANDERS

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1.–DEFINITION

(Synonym.—Farcy)

560.] Glanders is a contagious disease caused by a specific bacillus,
Pfeifferella mallei, affecting most frequently the equine species, from
which source human infections occasionally arise.

2.–AETIOLOGY

The disease is due to cutaneous or intestinal infection by *Pfeifferella* Causal
mallei derived from infectious discharges, artificial cultures, or infected organism
foodstuffs. It is extremely rare in countries where efficient control of
equine glanders is exercised. No case has occurred in England since
1927. Ostlers, grooms, farm-hands, and veterinary surgeons are particu-
larly liable to infection and usually manifest the disease with a skin
lesion. Artificial cultures are dangerous unless great care is taken; acute

fatal infections have occurred among laboratory workers. In rare instances infection has occurred from eating infected horse-flesh and by direct infection from an acute human case.

3.–PATHOLOGY

The bacillus is a straight or slightly curved rod 2 to 5μ in length and 0·5μ in breadth. The organism is Gram-negative, not acid-fast, and is often beaded. It is scanty in the lesions, unless there is an acute sero-sanguineous discharge. The bacillus grows readily on most laboratory media, but a visible growth is slow to appear. On potato medium a characteristic honey-yellow mucoid growth appears, and this becomes chocolate-brown after eight days. Inoculation of a culture into the peritoneum of a male guinea-pig causes suppurative infection of the tunica vaginalis. This reaction, known as the Straus reaction, is sufficiently specific for the identification of the organism when associated with the correct morphological and cultural characters.

*Straus
reaction*

The acute form of the disease in man is a bacteriaemia which, if not rapidly fatal, gives rise to abscess formation in the skin, muscles, lungs, or other internal organs, and occasionally may cause ulceration of the nasal mucosa, followed by perforation of the septum with a sero-sanguineous nasal discharge similar to that found in horses.

*Acute
glanders*

*Chronic
glanders*

In man the chronic form of the disease comprises nodular swellings which, if superficial, tend to break down and produce indolent ulcers having the characteristic histological structure of an infective granuloma with giant-cell system formation; in such lesions the organism is scanty. Nodular granulomas in the lungs sometimes remain inactive for long periods, but they are latent foci for an almost inevitable future exacerbation; they are about the size of a pea and are surrounded by a zone of congestion.

4.–CLINICAL PICTURE

*Cutaneous
glanders*

Skin infection is followed in two to six days by a nodular swelling with infiltration of the surrounding tissue; occasionally, at the onset, the swelling may resemble the papular stage of smallpox. The swelling soon ruptures, liberating a thin blood-stained discharge which later becomes thick ropy pus mixed with blood. Partial healing often takes place, but there is much destruction of tissue with cicatrization, and the bones may be invaded and destroyed. Usually the disease does not remain localized. Similar lesions appear in the skin and subcutaneous tissue in other parts of the body, associated with fever, acute muscular pain, and symptoms suggesting pyaemia. An acute infection of the nasal mucosa may occur, followed by destruction of the septum and, sometimes, otitis media. Localization often takes place in the lungs, as in the equine disease, and the nodules formed in the lung tissue or bronchial

*Spread of
disease*

*Nasal
infection*

*Infection
of lungs*

glands cause symptoms of an irregularly distributed broncho-pneu-
monia.

5.–COURSE AND PROGNOSIS

The course of the disease is very variable both in manifestation and *Acute form*
duration. Acute cases usually prove fatal in two to six weeks. On the
other hand, the acute attack may subside and the patient live for many
years with periodic exacerbations.

In the chronic form with deep-seated lesions, especially in the lungs, *Chronic form*
all clinical signs of activity may disappear for long periods. There may
be apparent recovery, but it is doubtful if the infection is ever eliminated.
Robins reviewed the course of a series of 156 cases and found survival
periods of from one to eleven years.

6.–DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The occupation of the patient should suggest the diagnosis. The specific
organism, which does not possess any very distinctive characters, is
extremely scanty in chronic lesions. Once a nodule has broken down,
secondary infection with rapidly growing cocci may prevent ready
diagnosis by culture. Stained films of the discharge should be made as *Culture*
well as cultures. The latter should be incubated for several days, as a
primary visible growth is slow to appear. A culture should be tested for
characteristic growth features and for Straus's reaction.

Blood cultures may be successful in acute cases. The blood-serum *Blood tests*
contains agglutinins and complement-fixing substances in the majority
of cases. Of these two tests the latter is the more reliable but should be
repeated at intervals, because the titre of the reaction varies from time
to time. Agglutinins to a titre of 1 in 1,000 to 1 in 2,000 are found in
the acute disease but tend to fall to a low level—less than 1 in 100—in
the chronic phase. (For technique of blood tests see BLOOD EXAMINA-
TION, Vol. II, p. 486.)

Sensitivity to mallein, a preparation of *Pfeifferella mallei* comparable *Danger of*
to tuberculin from *Mycobacterium tuberculosis*, is used as a test for the *using mallein*
latent disease in horses but is not applied to man, because of the danger
of precipitating an acute exacerbation.

Glanders in the human subject must be distinguished from necrotic *Diagnosis*
and pyaemic conditions of a chronic character due to other organisms *from other*
infections
which affect skin and bone. Syphilis and tuberculosis should be con-
sidered. In the acute phases differentiation must be made from enteric
fevers, acute rheumatism, acute osteomyelitis, and variola. Whitmore
described under the name of melioidosis a human disease which simulated *From*
glanders. The causal organism, *Pfeifferella whitmori*, belongs to the *melioidosis*
glanders group but can be readily distinguished by its motility. Meli-
oidosis is a natural disease of rodents and has occurred rarely in the

human subject in Rangoon, Malaya, Indo-China, and Ceylon, producing fever, broncho-pneumonia, and pyaemic abscesses (Stanton and Fletcher).

7.–TREATMENT

Preventive treatment

The prevention of glanders is accomplished by controlling the disease in equines. Modern methods of diagnosis in animals, including the mallein test, enable clinical and occult cases to be detected and the animals destroyed; and this is followed by disinfection of the premises. Persons who by their occupation are brought into contact with animals suffering from or suspected of glanders should be warned of the danger of human infection. Small cuts or abrasions should be covered and any small injury immediately treated with a cautery or a strong disinfectant.

Treatment of lesion

The surgical excision of a small local lesion in the early stages may prevent the infection from becoming generalized.

Specific treatment with serum or vaccine is not available. Numerous attempts have been made at chemotherapy without any outstanding success. Arsphenamine (salvarsan) and Bayer 205 (germanin) have been said to cause improvement.

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GLANDULAR FEVER

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1.–DEFINITION

(Synonyms.—Infectious mononucleosis; monocytic angina)

561.] Glandular fever is an acute infectious disease, characterized by fever, enlargement of the lymphatic glands, and changes in the blood,

Clinical groups

especially lymphocytosis and the presence of heterophil antibodies. The clinical manifestations and course are very variable, and three clinical groups may be separated: (i) glandular or Pfeiffer's type, occurring mainly in children of five to fifteen years; (ii) an anginose type, also known as 'monocytic angina'; and (iii) a febrile type, mainly in young adults, in which 'infectious mononucleosis' may be included.

2.–HISTORY

Glandular fever has had a prolonged struggle over many years for recognition as an entity *sui generis*. This is somewhat strange, as it occurs in considerable epidemics in schools and institutions and is not difficult to diagnose in such circumstances. It was first described by Pfeiffer in 1889, his account being confined to the glandular type. He recognized only the enlargement of the cervical glands, the involvement of the axillary and inguinal glands being first described by Desplats in 1894. Park West described an epidemic in America in 1896, and in 1897 Dawson Williams wrote the first article on the subject in Great Britain.

Pfeiffer's disease

Little interest was shown in the condition, and its existence as an entity was not accepted. During the Great War its existence was not recognized in any country, although it is now known that there were severe epidemics; but in 1920 Sprunt and Evans recorded under the title of 'infectious mononucleosis' a series of cases in which they had observed a transient and harmless lymphocytosis, although without recognizing its identity with Pfeiffer's disease, and in 1921 Tidy and Morley described a case of glandular fever in which a transient absolute lymphocytosis developed. The discovery of these blood changes afforded proof that glandular fever was a distinct entity, although its recognition advanced only slowly in the following decade.

'Infectious mono- nucleosis'

Relation to monocytic angina

During these years there was considerable discussion on the Continent about the nature of a condition known as monocytic angina, in which an absolute lymphocytosis was temporarily present, cases being usually recognized in infectious fever hospitals to which they had been sent with a diagnosis of diphtheria. Discussions were mainly of an academic character on the question of whether the cells were monocytes arising from the reticulo-endothelial tissues or lymphocytes from lymphoid tissue. The identity with glandular fever, which is now accepted, was not suggested. In England and in America the identity was accepted earlier. The full course of the febrile type was recognized in 1930, when there was an extensive epidemic in Great Britain.

Discovery of heterophil antibodies

In 1932 Paul and Bunnell made the interesting discovery that the blood in glandular fever contains heterophil antibodies, a phenomenon which apparently is almost pathognomonic of this disease.

3.–AETIOLOGY

The disease has been described in all temperate zones of the world, but *Geographical distribution* there are very few records of its occurrence in the tropics, and most of these are unsatisfactory, possibly due to the difficulty of diagnosis from the numerous other glandular enlargements which are common in hot countries.

The glandular type is commonest between the ages of five and fifteen *Age incidence* years. In adults it tends to be mild and abortive. The anginose and febrile types are commonest between the ages of fifteen and thirty years; they may also occur in younger children but are rarely of the same severity. Probably no age is immune to any of the types. The sexes are equally *Sex* liable.

There is some evidence that the causal agent may be a protozoon of *Causal agent unknown* the genus *Toxoplasma*, and by the injection of blood taken from a human subject early in the disease Bland produced pyrexia and lymphocytosis in rabbits and monkeys and transmitted the infection to a second generation; but further investigations are required. The earlier accounts of the isolation of various cocci may now be neglected.

The degree of infectivity is not high, and it is comparatively uncommon *Infectivity* for more than one case to occur in a household, although many examples to the contrary exist. Susceptibility appears to be almost universal; if two or three cases develop in a school, a high proportion of other children tend to be infected. It is possible that infectivity is almost confined to the earlier stages. It has been stated that sporadic cases tend to be more severe than those which occur in epidemics, but of this there is little evidence, and it is more probable that only the severer forms are diagnosed among sporadic cases.

4.–MORBID ANATOMY

Owing to the low mortality very few necropsies have been performed, and these have nearly all been on patients who have died from some septic complication. Most of the glands removed by biopsy have been from cases of the glandular type at the stage of lymphocytosis, and in *Glandular type* these the most marked change is lymphoid hyperplasia. Glands have been removed more recently from several cases of the febrile type and these show hyperplasia of the reticulo-endothelium. A gland removed *Febrile type* by Pratt in the later stage of this type mainly showed increased fibrous tissue and diminution of lymphoid tissue. There is not any reliable information on the condition of the bone marrow.

5.–CLINICAL PICTURE, COURSE AND PROGNOSIS

Three clinical groups may be described: (1) the glandular or Pfeiffer's type, (2) the anginose type, and (3) the febrile type. All intermediate forms

occur between these three groups, but most cases, whether sporadic or epidemic, can be placed in one or other of them.

(1)—Glandular or Pfeiffer's Type

The majority of cases in this group occur between the ages of five and fifteen years. No age is immune, and adults may contract the disease from children, but in such cases the attack is usually mild and abortive and is indeed often overlooked until direct inquiry is made.

Prodromal period   There is frequently a prodromal period of one to four days, during which there are the usual mild constitutional symptoms associated in childhood with pyrexia. There may be complaint of sore-throat, but nothing is visible on examination beyond a general reddening without exudation. The prodromal symptoms may be very mild and are often overlooked.

Glandular enlargement   Enlargement of the glands is often the first symptom to attract attention and may develop rapidly, a visible mass forming in the course of a few hours. In many cases it is at the onset mainly unilateral, a definite enlargement of the opposite side often developing later. Many observers have believed that it is commoner on the left side than on the right, but I have not observed any such difference in distribution.

Cervical   The cervical glands are specially affected, most characteristically those deep to the sternomastoid, about the middle of its length and somewhat below the angle of the jaw, and at this site there is frequently a large elastic gland which can be grasped between the fingers, the other enlarged glands being smaller. Any of the glands of the neck may be enlarged, and so also may be the pre-auricular, submaxillary, and submental lymphatic glands. The occipital glands are not often enlarged in this type. Oedema of the skin and tissues is very unusual, contrasting with its frequency in the early stages of mumps and in the anginose type. Pain and tenderness are very variable, and severe pain is rare. There is usually some degree of discomfort on moving the head, but there is often no pain and no tenderness on manipulation, especially in young children. Torticollis may develop at the onset in children and last for a few days, but is not serious.

Axillary   The axillary glands become enlarged in most cases, but usually later than the cervical glands and rarely to the same size. Enlargement of the
Inguinal   inguinal glands is less common, but they may attain a considerable size.

Mediastinal   It is probable that the mediastinal glands are often enlarged. A slight cough is common and has been attributed to the pressure of glands, as Pfeiffer mentioned in his original communication; this has been confirmed by radiological examination.

Salivary   It is doubtful if the parotid and other salivary glands are ever enlarged. I have never seen an instance, but Glanzmann recorded six cases during the large epidemic among children, which he watched in Berne.

Mesenteric   The mesenteric glands may enlarge and may even form a palpable mass

which entirely disappears as the infection passes. Severe constipation is sometimes a feature of an attack and may be due to this cause.

The spleen becomes enlarged in at least half the cases, but it is rarely *Spleen and* more than just palpable beneath the costal margin. The condition usually *liver* develops towards the end of the attack and may persist for long periods, even up to a year or more. The liver is less commonly enlarged but is occasionally distinctly tender.

There is usually some complaint of sore-throat for a day or two at the *Fauces* onset, but on examination little can be seen except a general redden- ing of the fauces and pharynx. Exudation is present only in subjects of previous tonsillitis. As Pfeiffer pointed out, the enlargement of the glands is out of proportion to the changes in the pharynx.

The temperature is usually slightly raised during the prodromal period *Temperature* and then rises sharply with the enlargement of the glands. The degree of pyrexia varies fairly closely with the amount of glandular enlargement, and the temperature tends to fall in the course of a few days as the main mass of the glands subsides. The temperature rises again with any recrudescence of enlargement of glands.

The constitutional symptoms are characteristically slight, even when *Constitutional* the temperature is high and the glands are greatly enlarged. The patient *symptoms* does not look or feel so ill as the size of the glands would suggest. Con- stipation is apt to be troublesome, and vomiting occasionally occurs. Epistaxis is not uncommon in growing children and may be sufficiently severe to cause anaemia and temporary anxiety.

The main mass of the glands usually diminishes rapidly in the course of three or four days, the temperature and constitutional symptoms subsiding at the same time. In most cases this is the end of the acute infection, although some glands may be palpable for several months subsequently, but recrudescences are by no means uncommon either *Recrud-* on the same or on the opposite side. Usually these are less severe than *escences* the initial attack, but occasionally the first attack is mild and the second the most severe. Recurrences occasionally extend over several weeks or even months. There is a tendency for an attack to be followed by a troublesome degree of debility which may last for six to twelve months, *Ultimate* but there are not any permanent ill effects, and the prognosis is uni- *prognosis* formly good except in the event of the rare septic complications.

(2)—Anginose Type

This type is much rarer than the glandular, and it is doubtful whether it should be described as a separate type or as a complication. The disease does not appear to spread in the anginose form, and it is possible that infectivity has passed before it develops. It is commonest between the ages of fifteen and thirty years, although it may occur at younger ages, but in small children it rarely attains the severity seen in young adults.

There is usually a recognizable prodromal period of one to three weeks *Prodromal* during which constitutional symptoms gradually increase in severity, *period*

and towards the end of the period there is complaint of sore-throat and discomfort in the neck. Less commonly the anginose type develops as a recrudescence following a mild initial attack of the glandular, but it rarely follows a fully developed attack. If the fauces are examined in the later stages of the prodromal period, the tonsils will be found to be red and swollen but without exudation, but more commonly a membrane is *Faucial* already present when the case first comes under observation. The mem-*membrane* brane forms with great rapidity and in appearance, colour, and distribution is indistinguishable from diphtheria. The uvula is often oedematous, and the membrane may extend on to it, but the membrane never involves the nose or larynx, and laryngeal obstruction is unknown. There is considerable peritonsillar oedema, but the formation of an abscess, which is due to secondary infection and may extend to the cervical glands, is rare.

Associated   Diphtheria bacilli are never present in the membrane, but Plaut-*organisms* Vincent's organism may be found.

Glandular   The cervical glands are always enlarged when the membrane is present, *enlargements* but they do not usually attain the size they have in the glandular form, and the characteristic glands beneath the sternomastoid are rarely palpable. Considerable oedema of the skin and subcutaneous tissues of the neck is common, and examination and movement may be difficult and painful. Usually there is some enlargement of the axillary glands, and the spleen is often palpable.

Constitu-   The temperature may rise to 104° or 105° F., and great discomfort and *tional* mental anxiety are present when the faucial symptoms are at their height; *symptoms* but in spite of this the patient often looks surprisingly well, and there is no tendency to collapse. Rashes are rare.

Course   The membrane may persist for many days, unlike that of diphtheria, but there is no increase in the constitutional symptoms. When the membrane separates, the faucial oedema diminishes, the temperature falls to normal or about 100° F., and the patient at once becomes more comfortable. Convalescence may now set in, but in other cases the temperature remains at about 100° F. for a week or two, and there may be slight recurrences, which do not attain the severity of the first attack.

Complica-   Pulmonary complications, including pneumonia, occasionally occur, *tions* and most of the instances of suppuration of the cervical glands in glandular fever have been in the anginose type of disease; but these complications are rare, and, although convalescence may be prolonged, recovery is nearly always complete without further anxiety. Diphtheria antiserum is valueless and may cause severe serum rashes.

(3)—Febrile Type

This may be regarded as the fully developed form of glandular fever. It occurs most typically in adults, although it is sometimes seen in children, usually in mild and abortive forms which contrast with the seriousness of the disease in adults. The characteristic course is illustrated in the chart (Fig. 125) and will be described in three stages.
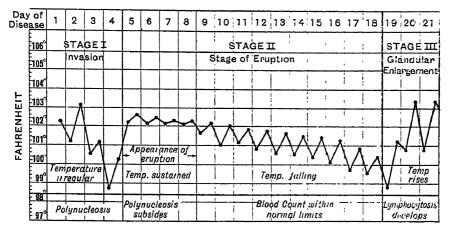
FIG. 125.—Temperature chart illustrating development of main features
in febrile type of glandular fever

(a) Stage of Invasion

This stage exhibits the constitutional features of a severe acute infection
without any pathognomonic manifestations. The onset is often acute,
although it may be insidious. There is general malaise, usually severe
headache, and not uncommonly conjunctivitis, but sore-throat is rare.
The temperature is raised but has not any regular course, the glands
and the spleen are not enlarged, and there are not any special gastro-
intestinal symptoms. This stage usually lasts from three to seven days
but sometimes longer.

(b) Stage of Eruption

The rash most commonly appears between the fourth and seventh *The rash*
days, usually on the fourth or fifth, but it may be delayed longer. The
usual rash may be described as a maculopapular eruption which often
resembles and may be indistinguishable from that of enteric fever. The
spots are about 2 to 5 mm. in diameter, pink or pinkish brown, scanty
in number, and distributed over the trunk and back; they disappear
on pressure. There is usually one crop which fades in about four days,
but further crops may develop or appear for the first time in a relapse.
A rash is not invariably recorded, but in my experience its absence in
adults is extremely rare. Occasionally the rash may assume other forms,
which will be mentioned later.

With the onset of the eruption the constitutional symptoms increase *Constitu-*
in severity, and the temperature rises to 102° F. or higher. There may be *tional*
recurrent rigors and profuse sweating. The temperature gradually falls *symptoms*
and may become normal, but rises with each return of the eruption.

This stage usually lasts about two weeks but may be considerably
longer. Towards the end of it the patient may be greatly exhausted,
especially if the sweating has been exacerbated by the administration
of antipyretics. The spleen is occasionally palpable towards the end of

Wassermann reaction this stage. The Wassermann reaction is not uncommonly positive during this stage.

(c) *Stage of Glandular Enlargement*

The glands usually enlarge towards the end of the third week, and the temperature then rises again to 102" F. or higher. The distribution of the glands affected is the same as that in the glandular type, but they do not enlarge to the same extent and are often found in a routine examination performed because of the rise of temperature.

Temperature Sore-throat is rare. The spleen usually becomes palpable in this stage. The temperature is usually remittent for about two weeks and then becomes intermittent and gradually falls to normal, the course corresponding approximately to the diminution in the size of the glands. The constitutional symptoms diminish concurrently, and the general condition improves, although considerable exhaustion remains.

Relapses common Recurrences and relapses are common and may lengthen the duration to many weeks or even months. The most severe cases are generally associated with comparatively slight glandular enlargement.

(4)—Blood Picture

Absolute lympho- cytosis The characteristic change in the blood-cells is an absolute lymphocytosis appearing concurrently with the glandular enlargement, but this does not represent the whole effect of the infection on the blood-producing tissues.

TABLE I.—Polynucleosis

AUTHOR	AGE	GLANDS PALPABLE	DAY OF BLOOD COUNT	LEUCO- CYTES	POLY- NUCLEARS PER CENT
Scheer	6 months	Onset	3	13,200	71
Tidy	9 years	2	4	31,000	79
			7	27,500	78
			20	10,300	30
„	9 „	Onset	2	15,600	76
			5	6,200	36
„	10 „	„	24*	19,000	73
Baldridge	19 „	„	2	·15,000	85
			9	6,400	73
			12	8,400	51
			21	7,700	37

* Relapse

(This and Tables II and V are modified from *The Lancet*, 1934)

Prodromal polynucleosis The first effect is on the myeloid tissues and is exhibited by a polynucleosis during the prodromal period (see Table I). In many cases the

figures are within the higher limits of the normal, but it is not uncommon to see a total count of 12,000 to 15,000 per c.mm. with 75 to 80 per cent of polynuclear cells. Higher figures may occur, such as a total of 30,000 with 80 per cent of polynuclears. Morphologically the polynuclear cells tend to show a shift to the left, i.e. towards more primitive cells with a less subdivided nucleus (see Vol. II, p. 479). Much more rare than polynucleosis is the development of a neutropenia, the total count falling to 3,000 or even 2,000 cells per c.mm. This leucopenia is almost entirely due to the reduction of polynuclear cells and thus results in a high relative lymphocytosis. The lowest recorded figure is 2,000 per c.mm., and probably glandular fever never produces a picture which could cause serious difficulty in the differential diagnosis from agranulocytosis. *Neutropenia and relative lympho-cytosis*

Both polynucleosis and neutropenia occur only in the initial stages and never develop during the course of the illness. They are transient, and within a few days the polynuclear cells are in the neighbourhood of normal and subsequently tend to vary round this point, being below rather than above it.

It is most important to be familiar with the occurrence of the early polynucleosis, as this feature has led to many errors of diagnosis.

The characteristic change in the mononuclear cells is the development of an absolute mononucleosis (see Table II). The mononucleosis reaches its maximum in the course of a few days from the initial rise and then diminishes, at first rapidly and later more slowly. In some instances the mononucleosis may persist for many months, a feature which has already been observed with regard to the lymphatic glands. The course follows approximately the enlargement and subsequent diminution in size of the lymphatic glands. *Absolute mono-nucleosis*

TABLE II.—Mononucleosis

AUTHOR	AGE	TOTAL LEUCOCYTES	MONONUCLEARS PER CENT
Feer – –	1 year	63,000	81
de Bruin – –	1½ years	63,000	78
Nelken – –	4 ,,	58,000	59
Feer – –	1 year	54,500	64
Price – –	7 months	44,000	84
de Lange – –	10 ,,	41,200	85

The morphology of the mononuclear cells is of interest. There has been much dispute whether the cells are lymphocytes from lymphoid tissue or monocytes from reticulo-endothelium, cells which are sometimes known as plasma cells. There is little doubt that cells are present from both these tissues and that abnormal lymphocytes cannot be clearly distinguished from abnormal monocytes. At the first evidence of lymphocytosis the cells usually do not differ greatly from normal, but within two or three days the predominant cell is usually a large mononuclear with clear cytoplasm, resembling a large lymphocyte but with a nucleus *Morphology* *Origin of cells*

which is less definite and is often referred to as foamy. The blood picture may change rapidly and may present numerous types of abnormal mononuclear cells, probably derived from both the lymphoid and reticulo-endothelial tissues. As convalescence sets in, small lymphocytes again predominate. The lymphocytosis may be recognizable many months after the glands have subsided and all symptoms have passed.

Changes in convalescence

Differences from lymphoid leukaemia

The blood picture in glandular fever thus differs from that of lymphoid leukaemia in several respects: (i) the predominant cell at the height of the infection usually resembles, although it is not identical with, a large lymphocyte, a type which is almost unknown in acute lymphoid leukaemia; (ii) numerous types of abnormal mononuclear cells are present simultaneously, in marked contrast to the uniform picture in lymphoid leukaemia; (iii) the picture often changes with great rapidity in the course of the case. The predominant cell may vary in different cases.

Eosinophils

The eosinophils may be reduced in the stage of polynucleosis and increase during convalescence.

Factors affecting blood picture

The general course of the blood changes and the blood picture will depend on the sum of the two factors, the changes in the polynuclear and the changes in the mononuclear cells. Both polynucleosis and lymphocytosis may sometimes be present together. Occasionally the polynucleosis may overlap for a short time the enlargement of the glands before the lymphocytosis has developed or, on the other hand, the lymphocytosis is sometimes recognized before the glandular enlargement.

Blood count

With regard to the number of cells, in patients over seven years of age a count of more than 20,000 is unusual, over 30,000 is rare, and from 40,000 to 50,000 is the maximum. As to the percentage of mononuclear cells, figures between 60 and 70 per cent are frequent, and up to 80 per cent common. All percentages over 90 are rare. Occasionally in infants the total leucocytes may rise above 50,000 at the onset, but in these cases the proportion of mononuclear cells is below 90 per cent. Figures which are common in lymphoid leukaemia, exceeding 50,000 cells and with 99 per cent of mononuclears, are never recorded in glandular fever.

Glandular type

In the glandular type the prodromal period is usually short and not severe; consequently the polynucleosis is rarely observed, as there is not any special indication for examination of the blood at this period. The lymphocytosis usually develops with the glandular enlargement but may reach its maximum a few days later and may persist after the glands have subsided. In cases with a high initial polynucleosis there may be a considerable interval before the lymphocytosis becomes evident. (See Table III.)

Anginose type

In the anginose type lymphocytosis is practically always present by the time the membrane has formed. In this type the prodromal period, although usually prolonged, has rarely attracted any special attention. (See Table IV.)

TABLE III.—Glandular Type

Course normal but somewhat prolonged in patient aged 12 years.

DAY OF ILLNESS	ERYTHRO-CYTES	HB PER CENT	LEUCO-CYTES	PN	PERCENTAGES OF			
					E	L	M	B
1	4,900,000	94	8,700	77	1	18	3	1
2	..	..	5,200	61	1	33	4	1
4	4,800,000	94	13,500	34	1	61	3	1
6	5,100,000	96	17,200	22	..	70	8	..
8	..	..	18,600	14	..	80	6	..
10	..	..	19,700	12	1	77	10	..
12	..	..	16,800	14	..	78	8	..
14	..	..	14,100	14	..	76	10	..
16	4,800,000	94	14,800	22	1	71	6	..
20	..	..	12,300	32	1	59	8	..
25	..	..	11,000	49	3	40	6	2
30	4,600,000	96	8,400	54	2	37	6	1
40	..	..	6,600	52	3	39	5	1
3 months	4,400,000	88	7,200	65	3	26	5	1
6 months	4,300,000	86	7,400	72	2	19	6	1

TABLE IV.—Anginose Type

Patient aged 22 years

DAY OF ILLNESS	ERYTHRO-CYTES	HB PER CENT	LEUCO-CYTES	PN	PERCENTAGES OF			
					E	L	M	B
1	4,500,000	86	22,400	11	..	81	8	..
2	..	..	28,000	8	..	81	11	..
4	..	..	26,400	10	..	81	9	..
6	4,300,000	84	21,200	12	..	79	9	..
8	..	..	16,700	22	..	66	12	..
12	..	..	12,100	42	2	47	8	1
16	4,800,000	88	8,300	39	1	53	6	1
20	..	..	9,500	36	2	54	7	1
25	4,800,000	86	8,200	46	2	44	7	1

PN = polymorphonuclear neutrophils   E = eosinophils   L = lymphocytes
                    M = mononuclears   B = basophils

In the febrile type there is evidence of polynucleosis during the stage *Febrile type* of invasion. During the stage of eruption the blood count often shows little change from normal. This is in accordance with what might be expected, as the stage of invasion and the stage of eruption together represent a long-drawn-out prodromal period. The mononucleosis develops in the third stage with the glandular enlargement, but in this

more lengthy type the correspondence is not so close as in the shorter glandular type. (See Table V.)

TABLE V.—Febrile Type: Typical Course

DAY OF ILL-NESS	AUTHOR	AGE	RASH (DAY)	GLANDS (DAY)	BD. CT. (DAY)	TOTAL LEUCO-CYTES	PN PER CENT	M PER CENT
5–10	Longcope	30	5	22	6	3,000	57	43
					7	3,400	60	40
					10	5,400	54	46
	Mills	19	..	16	7	8,200	42	52
11–15	Mills	19	..	16	14	8,200	41	53
	,,	20	8	20	15	14,000	48	52
	,,	21	8	20	15	Normal		
	Benson	..	6	10	11	14,700	18	82
	Tidy	26	4	10	12	33,000	5	95
					14	32,000	6	94
16–20	Longcope	30	5	22	16	9,800	44	56
	Tidy	30	5	24	16	7,000	70	30
21–30	Mills	19	..	16	21	12,000	29	65
	Longcope	30	5	22	22	8,800	29	71
	Tidy	23	6	15	23	11,600	34	66
	,,	19	4	18	24	11,700	36	64
	,,	40	5	24	27	13,000	43	57
	,,	26	4	10	27	29,000	12	88

BD. CT. · blood count   PN · polymorphonuclear neutrophils
M mononuclears

Mixed types Finally, there are mixed clinical types in which, for example, the glandular enlargement may precede the eruption, and in these no rule can be laid down for the course of the changes in the blood.

(5)—Rashes

A rash is rarely observed in the glandular type and is very rare after the membrane has formed in the anginose type, although it may have been present in the prodromal period. A rash is commoner in the febrile type and is present in most adults.

Maculo-papular variety There are two important varieties. The maculopapular variety has already been described (see p. 565) and may closely simulate the rash of enteric fever. The rubelliform variety may be indistinguishable *Rubelliform variety* from German measles and is possibly a confluent type of the former variety, being always discrete in parts. It is commonest in quite young children or infants, but either variety may occur at any age.

Other varieties of eruptions may occur which have been described as

erythema and urticaria, and the rash has been mistaken for those of *Other varieties*
typhus, measles, and other conditions.

The rash usually precedes the glandular enlargement, but in atypical *Time of appearance* clinical forms it may appear at the same time or later than the glands or during a recrudescence.

(6)—Variations in Clinical Types

Any combination of the three principal clinical types may occur. The *Combinations of types* course may be severe and prolonged with marked constitutional symptoms, the glandular enlargement in such cases often being slight and easily overlooked. Obscure cases occur with prolonged pyrexia, abdominal pain, and absolute lymphocytosis, but with impalpable glands. On the other hand, the pyrexia may last for a few days only, during which definite glandular enlargement and an eruption may develop and subside. Mild forms are not uncommon with slight clinical manifestations and glandular enlargement, such cases being recognized in epidemics or by a chance examination revealing the lymphocytosis. Abortive forms are also met with in adults, such as parents or nurses who have contracted the infection from children. There has been no proof of the diagnosis of glandular fever in atypical cases in the past, since doubtless there are other causes of lymphocytosis than glandular fever, but the discovery of heterophil antibodies (see p. 572) may in the future lead to more accurate diagnosis.

Glandular fever is common in America among medical students and *Infectious mono-nucleosis* nurses. This type is described as infectious mononucleosis and resembles a mild course of the febrile type.

The course of glandular fever in infants is often atypical and may *Infants* exhibit features of all three types in a short period.

(7)—Complications

It is extremely rare for the glands to suppurate. When this takes place, *Sepsis* it is usually in debilitated persons and can be attributed to secondary infection, for example, from pre-existing tonsillitis. In the anginose form the glands frequently appear to be on the point of suppurating, but this rarely occurs, although many of the recorded cases of suppuration have been in this type, and retropharyngeal abscess may develop. The rarity of suppuration or sepsis also applies to otitis media and similar complications.

Conjunctivitis of a dry catarrhal type is not uncommon in the early *Conjunctivitis* stages and subsides without further trouble.

The occurrence of haematuria in glandular fever has been recognized *Haematuria* since the first description of the disease. Its frequency has been exaggerated, for it is certainly a rare complication, not exceeding 5 per cent of cases, and large epidemics have been recorded without a single instance. Cases have been watched for many years, and in no instance has nephritis been known to develop.

Epistaxis is not uncommon and may be severe. It usually occurs at the *Epistaxis*

onset or before the enlargement of glands in the febrile type and is most frequent in early adolescence.

Other haemorrhages
Other forms of haemorrhage occur, such as purpura, but only very rarely. Rectal haemorrhage has been recorded.

Jaundice
Jaundice has been not uncommon in some epidemics, especially in the febrile type. It is very rare in children. It subsides without ill effects.

Meningeal symptoms
The headache and pain in the neck may be sufficiently severe to suggest meningitis, and it is possible that in rare cases the meninges are involved, as lymphocytes have been found in the cerebrospinal fluid.

Respiratory organs
A slight cough is not uncommon and may be attributed to the pressure of mediastinal glands. The pressure on a bronchus may be sufficient to cause collapse of a lobe. Pneumonia is rare.

(8)—Heterophil Antibodies

The remarkable phenomenon of the presence of heterophil antibodies in the blood was discovered by Paul and Bunnell in 1932 in the course of a routine investigation. Stated briefly, heterophil antibodies in human blood are agglutinins and haemolysins to sheep's red cells. Normal human blood may contain such antibodies in a titre not exceeding 1 in 8. After injection of horse serum the titre may rise to a high figure.

Presence in normal blood

In glandular fever the titre may rise as high as 1 in 4,096. The rise begins early and rapidly attains the maximum. The titre then begins to fall and may reach normal in six weeks but the high titre may persist to some extent for several months; recurrences and exacerbations of the clinical symptoms are, however, apparently not accompanied by a renewed rise in the titre.

Specificity of reaction
A large number of control tests have now been performed in numerous diseases and infections, and the reaction appears to be specific for glandular fever. Only one or two cases of clinical glandular fever have been recorded in which the titre failed to reach a diagnostic figure, and there have also been one or two cases of other diseases, including a severe purpura, which have given a high titre; but these exceptions are very few, and the presence of a high titre is almost pathognomonic of glandular fever. This test is now past the experimental stage and can be relied upon to establish the diagnosis in doubtful cases if performed during the acute stage. It has been carefully studied by many investigators, including Bailey and Raffel; Davidsohn; Beer; Stuart, Welch, Cunningham, and Burgess, who have found many interesting features in the serological reactions. Possibly the transient Wassermann reaction which has been observed is connected with the heterophil phenomenon. It may be noted that rabbits inoculated with blood from a case of glandular fever develop heterophil antibodies in high titre.

6.–DIAGNOSIS

Glandular fever is a febrile disease with general glandular enlargement and an absolute mononucleosis with special changes in the white cells,

and when these characteristics are present the diagnosis is usually simple. In cases of difficulty the test for heterophil antibodies can now be relied upon, but it may not be conclusive at the onset.

7.–DIFFERENTIAL DIAGNOSIS

(1)—Glandular Type

The diagnosis from acute lymphoid leukaemia is rarely difficult, since in *Diagnosis* glandular fever the patient does not appear ill and is not anaemic. The *from acute lymphoid* differences in the blood pictures have already been described (see p. 568). *leukaemia* The rapid recovery soon decides the diagnosis.

Mistakes in diagnosis from mumps are frequently made, and occa- *From mumps* sionally the decision may be difficult. In the glandular type oedema in the neck is extremely rare and pain usually slight. The parotid over the jaw is never enlarged.

The diagnosis from sepsis is occasionally difficult when there has been *From sepsis* a previous tonsillitis and exudate is present on the tonsils. The doubt rarely exists for more than a few hours.

(2)—Anginose Type

Glandular fever angina differs clinically from diphtheria in the long *From* prodromal period with slow onset of sore-throat, the comparatively mild *diphtheria* constitutional symptoms, the long duration of the membrane, and the absence of collapse. Lymphocytosis never occurs in diphtheria.

In scarlet fever the prodromal period does not exceed one or two days. *From scarlet*
Despite statements to the contrary it is not proved that Vincent's *fever and Vincent's* angina produces lymphocytosis. *angina*

(3)—Febrile Type

The clinical diagnosis from enteric and influenza may be difficult in *From enteric* the prodromal stages, but most of the mistakes were made before the *and influenza* febrile type was recognized.

With a rubelliform eruption the diagnosis from German measles may *From German* be difficult or impossible, especially in cases of glandular fever in which *measles* the occipital glands are enlarged.

8.–TREATMENT

The disease is undoubtedly infectious, and isolation is indicated, but the *Prophylaxis* degree of infectivity from a simple case is not very high. Epidemics are common in schools and institutions. It should be borne in mind that with reasonable precautions an ordinary case rarely infects other members of a household, but when two or three cases have occurred in a school a high proportion of the children commonly become infected.

Symptomatic treatment is, in general, sufficient. In the glandular type

Symptomatic treatment the patient should be confined to bed until the temperature has been normal for several days and the main mass of the glands has subsided. During the acute stage discomfort is eased by warmth to the neck, and the glands should be covered with cotton-wool.

In the prolonged febrile cases there may be marked exhaustion, and careful nursing is necessary. During convalescence there is often a distinct degree of debility, and tonics and iron are indicated over long periods.

Specific treatment useless Specific treatment with arsenical preparations and other methods have proved valueless, and diphtheria antiserum is useless.

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GLAUCOMA

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Reference may also be made to the following titles:

BLINDNESS   EYE EXAMINATION

1.–DEFINITION

562.] Glaucoma is not a disease but a symptomatic condition, the term being used to connote generally the composite congeries of diseased states which have the common feature that their clinical manifestations are to a greater or lesser extent determined by an increase in the intra-ocular pressure.

2.–INFANTILE GLAUCOMA

(*Synonyms.*—Buphthalmos; hydrophthalmos)

Aetiology   563.] This is an uncommon condition, due to a developmental anomaly in the region of the angle of the anterior chamber hindering the drainage of the intra-ocular fluid.

Pathology   Various pathological conditions may be found, of which the most pronounced are absence or defective formation of the canal of Schlemm and blockage of the angle by the failure of the root of the iris to separate from the corneosclera.

Clinical picture   Since the rise of tension occurs while the sclera is still plastic and extensible, this structure tends to give way, so that the globe increases in size. As the sclera is stretched it becomes thin, and the dark pigment of the uveal tract shines through it, giving it a bluish colour. The cornea is larger than normal, ruptures in Descemet's membrane and opacities in the interstitial tissue appear, the anterior chamber is deep, and the optic disc is deeply cupped.

Prognosis   The condition tends to be progressive, often to blindness.

Treatment   Treatment is very unsatisfactory, the only hope lying in operation, which very often must be repeated more than once. The operative methods are many, but probably the best are corneoscleral trephining with an instrument of large aperture, and large sclerotomies of the type advocated by Herbert.

3.–SECONDARY GLAUCOMA

(1)—Aetiology and Pathology

564.] In this class of case the tension rises as the result of some pathological condition occurring in the eye. In most cases the mechanism of the rise is either a blockage of the drainage channels at the angle of the iris or an increase in the viscosity of the intra-ocular fluid, so that, in both cases, the drainage of the aqueous humour is impeded.

Causes   The commonest causes of the condition may be grouped as follows:

Iridocyclitis   (i) Iridocyclitis, involving adhesion of the root of the iris to the back of the corneosclera; a blockage of the meshes of the angle of the anterior chamber by fibrin, leucocytes, pigment, and so on; and an increase in the albumin of the aqueous.

Synechiae   (ii) Anterior synechiae, adhesions of the iris to the cornea, due, for example, to a perforating wound.

(iii) Annular posterior synechiae, involving seclusion or occlusion of the pupil with the production of iris bombé.

Wounds of lens   (iv) Wounds of the lens, involving a swelling of this tissue, thus pushing the iris into contact with the corneosclera and, after a rupture

of the capsule has occurred, causing an increase in the albumin of the aqueous.

(v) Dislocation of the lens, pushing the root of the iris forward *Dislocation* towards the cornea. *of lens*

(vi) Intra-ocular tumour. In this event the cause of the rise of pressure *Tumour* is frequently obscure, but in some cases it seems to be associated with a blocking either of the angle of the anterior chamber or of the venous outflow from the eye.

(vii) Intra-ocular haemorrhage, in which again the cause of the *Haemorrhage* increased tension is frequently obscure but to some extent may be due to an increase in the colloid content of the intra-ocular fluid.

(2)—Treatment

The treatment should be directed to the causal condition. If this can be controlled, the rise of tension frequently subsides. For example, an iridocyclitis should be treated, and often in this event the beneficial effects of atropine on the cause of the inflammation will reduce the tension. An intumescent lens should be removed, and if mechanical obstructions to the intra-ocular fluid exist these should be corrected, an iris bombé by an iridotomy or an iridectomy, anterior synechiae by cutting them, and so on. If, in spite of this, the tension still remains high, causing pain or diminution of vision, operation directed to its relief is advisable. The type of operation varies with the condition which is present, but as a rule a wide iridectomy or a trephining meets the case.

4.–PRIMARY GLAUCOMA

(1)—Aetiology

565.] Primary glaucoma is a common disease, occurring essentially in *Incidence* elderly persons, particularly those of a nervous temperament. When it occurs in earlier life there is usually an hereditary element. It is commoner in women than in men and is equally prevalent in all grades of society, being apparently independent of hygienic conditions. A most important fact is that it is almost invariably bilateral, attacking, as a rule, one eye first. The second eye, even although apparently normal, should always be viewed with suspicion and carefully observed as a glaucoma suspect.

Despite an enormous amount of research, the cause of primary *Cause* glaucoma is unknown. It is obvious that it involves some upset of the physiological conditions which control the maintenance and variation *Physiological* of the intra-ocular pressure, and so long as these physiological processes *imbalance* are not certainly known their pathological aberrations must remain obscure.

The most recent researches on the pressure equilibrium of the eye suggest that the intra-ocular fluids are in equilibrium with the capillary blood, being formed in the main as a dialysate from them (Duke-Elder, *Relation to* 1927); it follows that the intra-ocular pressure is maintained at the level *capillary blood-* of the hydrostatic pressure in the capillaries less the difference between *pressure*

the osmotic pressures of the plasma and the aqueous humour. It also follows that it will be varied by those factors which alter either of these pressures or increase the volume of the contents of the globe. Further, it seems adequately established that in the healthy organ these changes are compensated within wide limits by the possibility of the escape of aqueous humour in greater quantity than is necessitated by the normal circulation of this fluid through the safety-valve action of the sinus venosus sclerae (canal of Schlemm) and the other venous exits; but in so far as this mechanism is rendered ineffective by pathological changes in these regions, these alterations in pressure tend to become cumulative and permanent.

Compens- atory mechanism

Considering these factors seriatim, a high general blood-pressure, in the light of the statistical evidence now available, must be absolved from any influence either as an essential or even an important factor in the aetiology of glaucoma.

Blood- pressure

The state of the capillary pressure, however, is more important, especially in the more acute aspects of the disease. The control of the capillary circulation is a complex and little understood matter, involving physical, nervous, chemical, hormonal, and psychical influences.

The tendency to acute glaucoma in persons of an emotional tempera- ment has long been recognized, and of recent years a large amount of attention has been devoted to the aetiological importance of the part played by the endocrine group of glands and their association with the sympathetic nervous system (Scalinci; Besso; Lagrange).

Endocrine control

In the most acute manifestations of the condition the nervous control of the uveal circulation is undoubtedly of great importance, for it has been recently shown that in this region a very obvious system of local axon-reflexes exists, so that a well-marked triple response, such as can be demonstrated in the skin, can be set in motion after trauma of the tissues (Duke-Elder, 1931). Thus, experimentally, when histamine is liberated in the eye, an acute attack of glaucoma can be produced, due to a generalized and massive dilatation of the uveal capillaries and a profuse transudation of a colloid-rich plasmoid fluid into the eye. It is probable that some such mechanism explains the acute phases of the disease.

Nervous control

So far as the question of osmotic pressure is concerned, the only finding of importance which has been noted with any degree of constancy is that the sodium chloride content of the blood and consequently the osmotic pressure of the blood of persons suffering from glaucoma are less on the average than those of healthy people (Hertel and Citron; Ascher). If this is found to be generally the case, it may well have an aetiological bearing; and if, superadded to this, some alteration of the permeability of the membranes separating the blood from the intra- ocular fluids develops (which has been experimentally confirmed), so that osmotic equilibrium at the abnormal level is not easily established, this factor may be of more than incidental importance.

Osmotic pressure

Permeability of membranes

An increase in the volume of the contents of the globe would without

doubt involve a rise of pressure in the eye, provided the exit channels *Increase in* of the intra-ocular fluid were impeded. A typical instance of such a *volume of contents* mechanism is seen in the secondary glaucoma associated with an intumescent lens. Any influence, however, which this may have in chronic primary glaucoma is very obscure. The vitreous gel is capable of swelling and shrinking (Duke-Elder, 1930); but conditions have not been established clinically which would tend to bring this about (Schmelzer; Schmerl; Hertel, 1921), and, moreover, it has been shown that the swelling pressure of the gel is insufficient to maintain the pressures which may be observed clinically (Davson, Duke-Elder, and Benham, 1936).

The classical hypotheses as to the aetiology of glaucoma concentrated *Blockage of* on a blockage of the drainage channels of the intra-ocular fluid in the *drainage* region of the angle of the anterior chamber. Thus Priestley Smith attributed a preponderant part to the lens: as the lens increases with age, the circumlental space is diminished, making the anterior chamber shallow and pushing the iris into contact with the corneosclera, thus occluding the filtration angle. Other hypotheses have been put forward suggesting factors which may disturb the efficiency of the escape of aqueous humour: the formation of peripheral synechiae, sclerosis of the pectinate ligament (Henderson), pigmentary accumulations in its meshes (Koeppe), a defective inward pull of the ciliary muscle (Herbert, 1925), and so on. It would appear, however, that while each or all of these may exert some influence, perhaps a deciding influence, the cause of primary glaucoma is something deeper and more subtle.

(2)—Pathology

The pathological features of most interest in an eye which has been subject to primary glaucoma are concerned with changes occurring at the angle of the iris and the optic nerve head. The latter region suffers earliest and most from the increased pressure. The lamina cribrosa is pushed backwards, first to form an anterior concavity and finally to be displaced backwards as a whole, while the nerve-fibres undergo atrophy, the two concurrent processes producing the appearance of a cup with overhanging edges at the optic disc. At the angle of the anterior chamber the iris is frequently opposed to the corneosclera, to which it eventually becomes firmly adherent, forming a false angle anterior to the true one, through which filtration of fluid is much impeded.

For the rest, the tissues of the eye show a general pressure atrophy *Atrophy* and degeneration, a process which involves the retina, the choroid, the ciliary body, and the iris. In the final stages of absolute glaucoma the atrophy may be extreme; the sclera gives way either at the ciliary region or near the equator, forming ciliary or equatorial staphylomas. Complete degeneration of the vascular tissues may lead to a final diminution of tension, and commonly, owing to the development of a progressively defective resistance, corneal ulceration of a virulent and intractable type occurs, and panophthalmitis may complete the picture.

(3)—Clinical Picture

(a) Chronic Glaucoma

Chronic glaucoma is an extremely insidious disease. It starts without symptoms and may run on for years without attracting attention, often being discovered in routine examination while the patient is quite unaware of anything amiss with his sight. When symptoms do become obvious the disease is invariably established. The symptoms which are usually noticed first are recurrent attacks of dimness of vision, lasting perhaps a few hours, and the appearance of coloured halos round lights, effects due to pressure oedema of the cornea during exacerbations of the intra-ocular tension. Ocular discomfort or frontal headaches may be evident, and loss of accommodation and diminution of the light sense may occur but are less obvious. At a later stage defects in the visual fields may become obvious to the patient.

Earliest symptoms

(b) Acute Glaucoma

Slight exacerbations in the symptoms are a constant feature of chronic glaucoma, and at any time, particularly in the presence of vasomotor instability, these may assume the dimensions of actual acute attacks. The attack may come on with great suddenness. The lids are oedematous; the conjunctiva is congested and oedematous with much ciliary injection; the cornea is cloudy and insensitive; the pupil is dilated, oval, and immobile; and the eye itself is stony hard. Ophthalmoscopic examination is usually impossible owing to the oedematous state of the cornea. Acute neuralgic pain is usually severe and may be associated with vomiting and considerable prostration. The vision is always impaired and may be rapidly abolished but is invariably permanently lowered with a contracted field after every acute attack.

Sequelae

(4)—Diagnosis

The diagnosis is made essentially on the state of the optic disc, the tension, and the visual fields. The typical glaucomatous eye is small, with a slightly dilated and sluggish pupil, owing to oedema and pressure on the ciliary nerves; an atrophic iris showing on slit-lamp examination considerable pigmentary disturbance; and a cupped optic disc with sharp shelving, over which the vessels are acutely bent.

Tension

The tension may be very deceptive, for the rise may be so slow, insidious, and subject to remissions that it may readily be missed. When there is doubt, repeated tonometric observations should be made, especially at different times of the day. In the normal individual the tension should not differ materially between the two eyes and should not vary within appreciable limits at different times of the day, on the adoption of the horizontal position, or on the administration of miotics or mydriatics, but it should be considerably lowered by a moderate amount of massage.

Diurnal variation

Whereas in the normal eye the diurnal variation in tension should not exceed a pressure of one or two millimetres of mercury, in the glaucoma-

tous state the cessation of muscular movements, which normally aid the drainage of the aqueous humour, induces a rise during the night, culminating in the early morning; conversely the activity of the day gives rise to a progressive fall to a minimum in the evening (Thiel; Hagen). Even although the absolute tension lies continually below the normal level, a diurnal variation of over 5 mm. Hg indicates some obstruction to the circulation of fluid. Moreover, when the regulating mechanism of the sinus venosus sclerae (canal of Schlemm) has become inefficient, the vascular congestion induced by decubitus may raise the tension some 6 mm. Hg (Thiel); the administration of physostigmine lowers the tension considerably, whereas a safe mydriatic, such as euphthalmin, raises it, the former by opening up, the latter by closing down, the already embarrassed drainage angle. Finally, massage, which should lower the tension of a normal eye by about one half, may have comparatively little effect (Colombo).

Perhaps the most important point in the diagnosis is the change in the visual fields: this, being a pressure effect, is obtained only in well- *Visual fields* established glaucoma. For this purpose the field is best explored on a 2-metre Bjerrum screen with a 1 mm. white object. This is merely a large screen of black cloth on which the meridians of the visual field are marked; while the patient fixes a target in the centre, a test object is moved over the screen and the patient is asked to say when it comes into view and when it disappears. One of the first signs is the pheno- menon of 'baring of the blind-spot' (Sinclair), a pathognomonic sign, *'Baring of* whereby the field for a $\frac{1}{2000}$ object, which should include the blind- *the blind-spot'* spot, becomes contracted, so that its margin blends with the blind-spot, especially in its outer and upper part. Such an early effect may be abolished by physostigmine—again a pathognomonic sign.

A later development is the appearance of an arcuate scotoma running *Arcuate* round from the blind-spot 10 to 20 degrees from the fixation spot, *scotoma* usually in the upper part of the field (Bjerrum scotoma), a defect which frequently extends round to the nasal side and produces the typical nasal step in the field, terminating abruptly on the horizontal meridian.

The acuity of central vision may remain unimpaired for a very long *Central* time while the field gradually constricts; but eventually only a small *vision* segment of temporal field may remain, and, finally, as pressure atrophy of the visual elements becomes complete, all perception of light is lost.

(5)—Treatment

(a) Chronic Glaucoma

The treatment of glaucoma is essentially surgical, directed towards the establishment of permanent drainage in order to relieve the tension. Although this is so, and although more harm is done by delaying surgery than by operations improperly performed, the medical treatment of glaucoma is important, for there are certain conditions in which it *When to* is advisable to postpone surgery, or in which it may be avoided entirely. *delay* The chief reason for this will be extreme age or infirmity of the patient. *operation*

Medical treatment is, however, merely a temporary palliative and can never cure the disorder.

Medical treatment

Miosis

Miosis can usually be produced by 1 per cent solution of pilocarpine nitrate or 0·25 per cent solution of physostigmine salicylate; there is seldom any reason for employing stronger miotics, the unpleasant effects of which would become intolerable after a time. In some cases

Tonometry

this effect may continue indefinitely. It is important to estimate progress by often measuring the visual fields and to remember that the tension varies during the day in glaucoma patients, so that one whose tension is always normal when seen may at other times, especially during the night, have higher tension which will cause gradual deterioration of the fields. Hence tensions should be measured at various times of the day, especially early in the morning before any miotics have been used. The danger of miotics is over-confidence in their effect, and a patient using them must be under constant surveillance. When the use of miotics fails to control tension and fields, operation should be advised.

In special conditions demanding delay other measures become necessary. The most important agents at our disposal in such cases are

Adrenaline

adrenaline and its derivatives, administered as cotton-wool packs in the upper fornix (Gradle) or as laevo-glaucosan (Hamburger). Adrenaline is contra-indicated in acute glaucoma and whenever inflammation is present: even in chronic simple glaucoma it is not always entirely without danger. Many other drugs with a similar action have been suggested during the last few years. Tenosin, a compound of histamine with *p*-hydroxyphenylethylamine, a derivative from ergot, is favourably mentioned by von Hofe. Histamine is a powerful miotic and occasionally is useful either as a 2, 7, or 10 per cent solution of the hydrochloride (amino-glaucosan). Ergotamine was suggested by Thiel for chronic glaucoma, the great advantage of it being that it can be administered by the mouth over long periods. It is said to produce a considerable fall of tension and to act strongly as a miotic, the rationale of its action, according to Thiel, being a paralysis of the sympathetic nerves in the eye. It should be emphasized again, however, that the only rational view to adopt with regard to these drugs is to consider them as temporary expedients, postponing but not without special reason replacing operation.

Operative treatment

Rationale of operations

Many different types of operation have been recommended for glaucoma: the majority of them depend on the establishment of permanent drainage between the anterior chamber and the subconjunctival space by cutting out a piece of the sclerotic, either by scissors (Lagrange), a trephine (Elliot), or a knife (Herbert), so that a gap is left between the lips of the wound, which eventually becomes filled with loose scar tissue and remains as a filtering cicatrix.

The operation most usually performed at the present time is trephining *Elliot's* (Elliot's operation), in which a circular disc is cut from the wall of the *operation* globe by a 1·5 or 2 mm. trephine in the region of the limbus under a conjunctival flap. The knuckle of iris which prolapses into the wound is excised, so that an iridectomy is done at the same time.

In Lagrange's operation an iridectomy is performed, and, the con- *Lagrange's* junctival flap being left intact, a small piece of the anterior lip of the *operation* wound is snipped off.

In Herbert's operation a rectangular trap-door is cut in the sclera *Herbert's* immediately outside the limbus with the knife towards the cornea. *operation*

A modified operation is iridencleisis, in which the iris is incarcerated *Iridencleisis* in the wound to prevent its complete closure by cicatrization; a further modification—cyclodialysis—involves the establishment of drainage *Cyclodialysis* into the perichoroidal space by loosening the attachment of the ciliary body at one point.

Of all these types trephining probably produces the best results; but even it is uncertain, and if dense cicatrization develops it may have to be repeated. Moreover, it is not without danger, either immediate (such as failure or delay in the re-formation of the anterior chamber) or remote (development of cataract, late infection).

(b) Acute Glaucoma

In acute glaucoma the lowering of the tension as a preliminary to *Preliminary* operation reduces the risks of serious complications, gives time for *lowering of* arrangements to be made so that the operation can be done in the best *tension* circumstances, and makes the surgeon's work much easier and more certain of a satisfactory result. The line of conduct will depend upon how early the case is seen. When the condition has existed for several days, operation can almost never be avoided and should not be delayed longer than the few hours necessary for the proper preparation of the patient. Physostigmine salicylate 1 per cent should be instilled several *Physostig-* times at intervals of a minute, and this may be repeated at half-hourly *mine* intervals. Adrenaline is contra-indicated. The use of morphine is *Morphine* usually indicated for pain, and its miotic effect aids that of physostig-mine. A saline purge may be of use by depleting the body fluids and so exercising an indirect osmotic effect on the intra-ocular fluids. A much more dramatic effect is obtained by the intravenous injection of *Saline* concentrated (30 per cent) saline (30 c.c.) or of 50 per cent glucose *injection* (100 to 150 c.c.) (Duke-Elder, 1925). A further extremely useful expedient is the application of leeches to the temple. Not more than a *Leeches* few hours should be lost in such procedures, however, in such a late case, and reliance must be placed on the reduction of tension on the operating table by retrobulbar injections of procaine-adrenaline (4 *Retrobulbar* minims of 1 in 1,000 adrenaline hydrochloride solution added to a *injection* syringe containing 1·5 c.c. of 4 per cent solution of procaine hydro-chloride). Ten or fifteen minutes after such an injection it is not uncommon to find the tension reduced 10 to 20 mm. Hg or even to

normal. It is also the only means of assuring good local anaesthesia in acute glaucoma, in which formerly it was often necessary to use general anaesthesia.

In a case seen during the first twenty-four hours of the attack there is more hope of reducing the tension to normal, so that operation can be done under more favourable conditions, and more time can be spent upon the attempt. At the worst it is well to remember that there is one relatively minor procedure which may be successful in aborting an acute attack when operation is impossible or must be delayed too long *Paracentesis* for safety —namely, a simple paracentesis by a small limbal puncture. This may be done at home with little equipment and is much less dangerous than the alternative of a posterior sclerotomy.

If the tension can be brought down and maintained at a relatively low level, the eye may be treated until the stage of acute congestion has passed off, when a trephining operation can be performed. Alternatively, *Iridectomy* an iridectomy, as first introduced by von Graefe in 1856, is the operation of choice. The iridectomy must be large and basal in nature, so that a considerable segment of the iris is torn, not cut, from the ciliary body, thus opening up the angle of the anterior chamber. The prognosis of this operation, if performed early, is so good in acute glaucoma that it should be used unhesitatingly.

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GLÉNARD'S DISEASE

See VISCEROPTOSIS

GLOSSITIS

See MOUTH DISEASES

GLYCOGEN DISEASE

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1.–DEFINITION

(Synonyms.—Von Gierke's disease; hepatonephromegalia glycogenica;
thesaurismosis glycogenica)

566.] Glycogen disease is a congenital disorder of metabolism, characterized by an excessive accumulation of glycogen in the tissues. It was first recognized by von Gierke, who in 1929 reported two cases in which enlargement of the liver and kidneys was found at necropsy to be associated with abnormal deposition of glycogen in these organs. He suggested the name hepatonephromegalia glycogenica; but, although subsequent reports have shown that the liver is almost invariably involved, enlargement of the kidneys is by no means constant. Since other organs, e.g. the heart (cardiomegalia glycogenica), have been found affected, the names glycogen disease or von Gierke's disease are those most generally applicable.

2.–AETIOLOGY

Although a number of experimental investigations have been made by Schönheimer; Beumer and Löschke; Junkersdorf; van Creveld; Unshelm; and others, the aetiology of glycogen disease is not yet established.

The condition appears to be congenital and may be familial. The *Incidence* occurrence of a significantly higher incidence of cousin-marriages among the parents of affected patients than is normal in the general population has suggested the possibility that the defect is transmitted as a Mendelian recessive.

The condition is widely distributed, as in the few years during which *Geographical* it has been recognized cases have been reported from Germany, Holland, *distribution* America, England, Australia, Chile, and other countries. With the possible exception of Bauza's two Chilean cases, however, the condition does not appear to have been noted in the Latin races.

3.–PATHOLOGY

The biochemical findings are characteristic. Glycogen is not only stored in the tissues in excessive amount but can only with difficulty be liberated into the blood-stream as glucose. This results in a consistently low figure (usually 0·06 mgm. per 100 c.c. or less) for the fasting blood-sugar. *Blood-sugar*

The defective liberation of glycogen is well shown by the adrenaline test (see Fig. 126). Whereas in the normal child the injection of 5 minims of a 1 in 1,000 solution of adrenaline hydrochloride results in a rise of blood-sugar of at least 30 mgm. per 100 c.c. in half an hour, in the patient with glycogen disease the rise is much delayed, slight in amount, or altogether absent.

Adrenaline test

It might be expected that, with the blood-sugar at hypoglycaemic levels, symptoms of hypo-
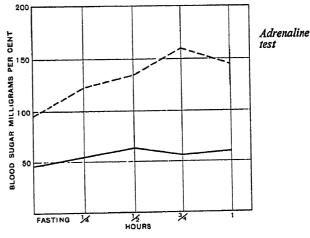
FIG. 126.—Effect of injection of 5 minims of a 1 in 1,000 solution of adrenaline hydrochloride on blood-sugar of patient with glycogen disease ——, and of normal control of same age ----. (By courtesy of Dr. W. W. Payne)

glycaemia, such as incoordination and convulsions, would be common *Absence of* in glycogen disease, particularly after exercise, when the demands for *hypo-* available glucose are increased, but this is seldom seen. Convulsions *glycaemic* have occurred in a few of the recorded cases, and others have shown *symptoms* lassitude and emotional instability. Usually, however, these patients are able to take active exercise without provoking symptoms. Nevertheless, it has been suggested that the retardation of growth, so common in glycogen disease, may be related to the prolonged starvation of the tissues in regard to available glucose.

Blood-glycogen

Van Creveld showed that the glycogen content of the blood was raised in glycogen disease as compared with normal controls; this was confirmed by Ellis and Payne, who also found that there was much more glycogen in the blood-cells than in the plasma. It was also shown, however, that the blood-glycogen content was considerably raised in some pathological conditions other than glycogen disease; so too much diagnostic importance should not be attached to this estimation.

Defect of storage

That some defect occurs in the storage of glycogen as well as in its liberation is shown by the fact that the blood-sugar tends to rise abnormally high and to fall slowly after ingestion of a glucose test-meal. Unlike the diabetic curve, however, the blood-sugar returns to an hypoglycaemic level.

Metabolism of fat

A secondary effect of the abnormal stability of the glycogen stores is an interference with the metabolism of fat. This is shown by the appearance of acetone in the urine in circumstances of normal life, i.e. in the absence of those factors tending to produce ketonuria in normal children. The blood-cholesterol is also raised.

A curious finding in a case recently described by Naish and Gumpert was the presence of much undigested starch in the stools, which were acid in reaction and contained amylase; the latter was normally active when the reaction of the stool was made alkaline. The stools have not, however, been noted as being abnormal in other instances.

Some hypotheses

As regards the nature of the defect of glycogen metabolism, it may suffice to mention some of the hypotheses that have been advanced, as none of these can be regarded as proved. Thus it has been suggested that an abnormally stable form of glycogen, differing in kind from normal glycogen, is deposited in the tissues; but this hypothesis has not been supported by subsequent investigations. Again, it has been suggested that the glycogen has an abnormal linkage to protein, rendering it peculiarly immobile; and that the ferment responsible for the breakdown of glycogen in the tissues is defective. Van Creveld compared the condition to a persistence of the foetal state. Recently Naish and Gumpert discussed the possibility that there was a local abnormality of tissue reaction, interfering with the normal splitting of glycogen. Hertz's suggestion that the condition is due fundamentally to dysfunction of the pituitary is attractive in many ways, particularly as these patients have been shown to be hypersensitive to insulin and are frequently retarded in growth and development. Up to the present time, however, no conclusive evidence has been produced in favour of any of these hypotheses.

4.–MORBID ANATOMY

This has been studied in the few cases that have come to necropsy owing to intercurrent infection, and in some instances material obtained

Liver

by operation has been examined during life. The liver has been found enlarged, smooth, and red or reddish-brown in colour. Fibrosis has not

been increased. The liver cells have been shown histologically to be enormously distended with glycogen, staining red with Best's carmine. For the identification of the glycogen, sections must be placed directly into an alcoholic solution, although even in aqueous solutions and for some considerable time after death the glycogen has been found to be more stable than normal. In some cases fat droplets have also been present within the liver cells.

The other organs involved have shown a similar histological picture, *Other organs* the cardiac muscle-fibres being almost unrecognizable owing to their distension with glycogen (Pompe; Antopol, Heilbrunn, and Tuchman). In the cases of nephromegalia the cells of the tubules were principally affected.

No constant abnormality of the endocrine system has been described, *Endocrine* although in two instances (one of von Gierke's original cases) the *glands* adrenals appeared atrophic.

5.—CLINICAL PICTURE

There are few characteristic symptoms; the patients usually come under observation in the first instance on account of the large size of the

Fig. 127.- -Glycogen disease with infantilism in two sisters aged 10 and 12 years, with normal control aged 8. (By courtesy of Dr. H. Thursfield)

abdomen or of delayed growth. In other cases the occurrence of convulsions, an intercurrent infection, or the familial incidence has led to a medical examination and recognition of the disorder.

The outstanding physical sign is the hepatic enlargement, the liver being smooth, firm, not tender, and often extending below the umbilicus. The anterior notch may be so deep as to cause the left lobe to be mistaken for the spleen. The latter, however, is not enlarged. There is no ascites, and seldom is there any distension of the superficial abdominal veins. In some cases there have been single transient attacks of jaundice, but this symptom is never permanent and is not characteristic of the disease.

Growth
Growth and genital development tend to be greatly delayed, particularly in later childhood. Although patients may be of normal proportions at birth, they generally lag behind children of their own age until the discrepancy in development becomes such that they may be said to show several years' infantilism, retaining the physical and emotional characters of much younger children (see Fig. 127). In such cases genital development and secondary sexual characters fail to make their appearance, although occasionally the condition becomes less marked with increasing age, and when adult life is reached the patients may be apparently normal.

In those cases in which organs other than the liver are involved, e.g. the heart or pylorus, symptoms are liable to arise from the visceral enlargement; interference with function is then primarily mechanical.

6.–PROGNOSIS

The prognosis as regards life in glycogen disease is relatively good, although a number of these patients have succumbed to intercurrent respiratory or other infection, and some of those in whom the cardiac muscle was involved have died with cardiac failure. Retardation of growth and development is usually progressive; but Worster-Drought's patient, probably an example of this disease, appeared essentially normal by the age of twenty-five, although the onset of puberty had been much delayed. In some instances the condition affects the younger siblings less severely than the elder.

7.–DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of glycogen disease can be made during life from the association of the above clinical and biochemical findings. A greatly enlarged smooth non-tender liver, not associated with splenomegaly or other evidence of cirrhosis, occurs in practically no other condition in childhood except hypertrophic steatosis (see below), and, very rarely, diabetes mellitus.

Diagnosis
from malig-
nant disease
Malignancy, e.g. hepatic metastases from an adrenal neuroblastoma, can be excluded by the slow course and slight interference with the general health seen in glycogen disease. Retardation of growth and a

familial incidence of the condition will be confirmatory evidence when present, although it should be remembered that familial cirrhosis with infantilism has been described. Cirrhosis, however, will almost invariably give rise sooner or later to some degree of splenic enlargement, to a liver that feels abnormally hard or irregular on palpation, and usually to secondary disturbances, such as ascites, jaundice, and distension of the superficial abdominal veins. The biochemical findings in glycogen disease, namely, a low fasting blood-sugar, defective response to adrenaline injection, an abnormal glucose-tolerance test, continual acetonuria, raised blood-cholesterol, and raised blood-glycogen are also characteristic when existing together. *From familial cirrhosis*

The condition likely to cause most confusion is one described by Debré and Semelaigne as hypertrophic steatosis, in which the infiltrating substance causing hepatomegaly is fat instead of glycogen. These authors include both this condition and glycogen disease under the heading of 'hépatomégalies polycoriques' (πολύς, much; κόρος, surfeit), a description coined to indicate excessive infiltration of the liver, but there seem to be good reasons for maintaining a distinction. Hypertrophic steatosis does not show the complete biochemical picture of glycogen disease, although some of the findings, for example, acetonuria and a low fasting blood-sugar, may be common to both. There is likely to be more disturbance of the general health in hypertrophic steatosis, and its onset may be more closely associated with infection. It must be admitted, however, that in some instances necropsy or biopsy of a portion of the liver provides the only conclusive method of distinction. *From hypertrophic steatosis*

Similarly, in those rare cases of diabetes mellitus in childhood in which great enlargement of the liver is associated with infantilism it is uncertain whether the hepatic enlargement is due to accumulation of fat or glycogen or both. Clinically, however, the condition is characterized by the other symptoms of diabetes if insulin is withheld, by glycosuria, and by a diabetic type of glucose-tolerance test. *From diabetes mellitus*

8.–TREATMENT

Little can be said with regard to treatment so long as the underlying pathogeny of the condition is so little understood.

In view of the low fasting blood-sugar it appears reasonable to give these patients a relatively high carbohydrate diet, with the carbohydrate well spaced throughout the day. *Carbohydrate diet*

Van Creveld used choline in daily doses of 30 to 600 milligrams in two patients and found a diminution in acetone excretion and elevation of the fasting blood-sugar in one of them. He found that thyroid treatment was useless. The injection of a potent anterior pituitary extract might well be tried experimentally in those cases in which there is well-marked infantilism. *Choline*

Endocrine therapy

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GLYCOSURIA

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Reference may also be made to the following titles:

ALKAPTONURIA   DIABETES MELLITUS

567.] The detection of sugar in urine and its significance are of great importance in both the diagnosis and treatment of diabetes mellitus.

1.–DIAGNOSTIC TESTS

(1)—Benedict's and Fehling's Tests

The reducing substance most often found in urine is dextrose (glucose); but other sugars, laevulose (fructose), lactose, and pentose, and substances like uric acid, creatinine, glycuronates, and salicyluric acid may be present in sufficient amounts to cause alarm. Homogentisic acid, which is excreted in that very rare condition alkaptonuria, is often mistaken for a sugar. Two tests are in use for the routine examination of urine, those with Benedict's and Fehling's solutions; both depend on the reduction in an alkaline solution of cupric sulphate to cuprous oxide.

Benedict's test

Benedict's solution, which is always ready for use and keeps indefinitely, contains anhydrous sodium carbonate 100 grams, sodium citrate 173 grams, and copper sulphate 17·3 grams in water to 1 litre. It is the more reliable of the two solutions, and the change of colour from blue to yellow or red is practically diagnostic of the presence of sugar. A change to a turbid green colour may be due to substances other than sugar; if the solution turns green but remains transparent, sugar is probably not responsible for the change. The test is usually performed with 5 c.c. of solution and 8 drops of urine (about 0·25 c.c.) but half these amounts can be used. The solution should be boiled over a flame for two minutes or placed in actively boiling water for five minutes. The solution will have changed colour in this time if moderate amounts of sugar are present, but, if the amount of sugar is very small, it is necessary to allow the solution to cool for ten minutes, to see if a yellow precipitate falls to the bottom of the test-tube. A white or greyish white precipitate may be caused by excess of phosphates in the urine and is not of any significance. It is essential to test new bottles of the solution with a little dextrose, as the solution used for estimating the amount of sugar quantitatively is similar in appearance but does not show any change in colour unless more than 2 per cent of sugar is present in the urine, when the solution becomes colourless with a thick white precipitate.

Fehling's test

Fehling's solution is still much used, as the test is carried out more quickly and the results are striking when large amounts of sugar are present. It is unreliable when the urine contains only small amounts of sugar, since the results are difficult to interpret. The solution should not be kept ready for use, as it deteriorates and, in course of time, may reduce by itself when boiled. The testing solution is prepared by mixing equal quantities of the solutions A and B, and these should be accurately measured. Solution A contains 34·65 grams of copper sulphate in a mixture of 0·5 c.c. of sulphuric acid and sufficient water to produce 500 c.c.; solution B contains 176 grams of Rochelle salt and 77 grams of sodium hydroxide in water to 500 c.c. If too much of the alkaline solution is added, small amounts of sugar will be destroyed before the cupric sulphate can be reduced. The solution is also likely to give greenish precipitates due to the action of the alkali on the urinary pigments. These defects make it an unsuitable reagent for the detection of small amounts of sugar, and patients with diabetes mellitus should not be taught to use it, because they may be misled by doubtful green tests. As neither Benedict's nor Fehling's test does more than show the presence of a reducing substance in the urine, the three other tests must be used in order to determine its nature.

(2)—Other Tests

(a) Fermentation with Yeast

Test for dextrose and laevulose

This is the simplest and most useful in clinical work, as only dextrose and laevulose give a positive result. The test must be carried out with the following precautions: (i) the urine must first be boiled and then

allowed to cool to a temperature of 37˚ C. in order to kill all organisms which ferment sugar and to get rid of all gases in the solution: and (ii) the yeast must be carefully washed to remove all sugar. and two control tubes should be put up—one containing distilled water and yeast to make certain that the yeast does not contain sugar. and the other water. yeast, and sugar to show that the yeast is active. The three tubes are placed in a water-bath set at a temperature of 37˚ C. with a thermostat or, if this is not available, in a beaker of water heated to this temperature and placed in an incubator at 37˚ C. It is important to keep the door of the incubator shut during the whole of the experiment. If the test is positive, gas will appear within three to four hours.

(b) Polarimetric Tests

When the fermentation test is positive, thus showing the presence of glucose or laevulose, the distinction between the two is easily made by the polarimeter if more than 1 per cent of sugar is present. When smaller amounts are present, the polarimeter cannot be relied upon, as glycuronates or β-hydroxybutyric acid may cause a laevo-rotation which exceeds the dextro-rotation due to the dextrose. In these circumstances the proof of the nature of the reducing substances is obtained by Seliwanoff's test (see below). *To distinguish between glucose and laevulose*

Two other reducing substances which are not fermented by yeast cause the rotation of polarized light—lactose, which is dextro-rotatory, and the pentose group, some members of which are dextro-rotatory and some neutral. The polarimeter is of use in confirming their presence, but the special tests described below are of more value. *Other rotatory substances*

(c) The Osazone Test

This is not of great value in clinical medicine, as it is given by dextrose, laevulose, lactose, pentose, and the glycuronates. The wheatsheaf crystals of dextrose, laevulose, pentose, and the glycuronates are similar when examined under a microscope, although the melting points of the pure substances are different. The crystals of lactosazone are difficult to prepare when only small amounts are present, but, if the preparation is successful, they have a characteristic hedgehog form. *Form of crystals*

(3)—Special Tests

(a) Seliwanoff's Test; Borchardt's Modification

A few crystals of resorcinol are added to equal quantities of urine and 25 per cent hydrochloric acid, and the solution is brought to boiling point and then cooled. If laevulose is present, a red colour will develop. The mixture is then neutralized by the addition of solid sodium carbonate and shaken with 3 c.c. of acetic ether or amyl alcohol. If laevulose is present, the solution will be yellowish-red with a weak green fluorescence and will turn rose-red on the addition of absolute alcohol. *Test for laevulose*

(b) Tollen's Test for Glycuronates and Pentoses

Spectroscopic examination

A knife point of phloroglucin is added to equal quantities of urine and concentrated hydrochloric acid. The solution is mixed and placed in a boiling water-bath and carefully watched. If glycuronates or pentoses are present, a cherry-red colour will develop. The solution on spectroscopic examination should show a band between the D and E lines (for spectra see Vol. II, Plate VI, facing p. 499). The solution is then cooled and centrifuged, and 3 c.c. of absolute alcohol are added to the supernatant solution. The mixture will be red and show the same band.

(c) Bial's Test

Distinction between pentoses and glycuronates

Bial's test is used to distinguish between pentoses and glycuronates; 5 c.c. of the reagent (1 gram of orcinol, 500 c.c. of concentrated hydrochloric acid, and 2 c.c. of 10 per cent ferric chloride) is boiled thoroughly, and 5 drops of urine are added. A green colour will develop slowly on standing if a pentose is present. The solution shows two absorption bands, one between C and D and the other near the D line.

Spectroscopic examination

2.—THE CLINICAL SIGNIFICANCE OF THE REDUCING SUBSTANCES

Dextrose

568.] Dextrose appears in the urine either because the blood-sugar is increased in amount, or because the threshold of the kidney is set at a lower level than 180 mgm. per 100 c.c. arterial or capillary blood or 150 mgm. per 100 c.c. venous blood. The differential diagnosis between these two conditions is described elsewhere (see Vol. III, p. 649).

The threshold of the kidney is lowered in many healthy people, and the condition is only discovered in the course of a routine examination. It has been detected in a child of ten months and is believed to persist throughout life. It is often present in several members of a family and is a dominant character, as the children of a renal glycosuric may have the same condition; the incidence is increased by first-cousin marriages (Graham). The amount of sugar passed depends on how much the threshold of the kidney is below the normal level. In many cases the excretion is less than 5 grams a day, but in some cases 20 to 30 grams may be excreted. In one such case the blood-sugar was lowered to 50 mgm. per 100 c.c. with insulin, but 0·5 gram of sugar was excreted every half-hour for the next $1\frac{1}{2}$ hours. The threshold is temporarily lowered in some women during menstruation and in the course of pregnancy. Once the diagnosis is established the condition does not require any treatment, and many Life Assurance Offices now accept these patients at normal rates. It should, however, be recognized that the presence of a lowered threshold would not prevent the development in after years of a true diabetes mellitus, although this has not been observed in any of my patients, some of whom have been under observa-

tion for twenty years. The treatment of diabetes mellitus is sometimes complicated by the presence of a lowered threshold. In these cases little or no trust can be placed on qualitative urine tests, and it is necessary to make numerous estimations of the blood-sugar or to estimate the total excretion of sugar in the twenty-four hours.

Laevulose is dealt with in the body in a different way from glucose *Laevulose* and does not cause so great a rise in the blood-sugar. In healthy persons a dose of 50 grams of laevulose does not raise the blood-sugar more than 30 mgm. per 100 c.c. in half an hour, and the blood-sugar returns to its normal level in two hours. The difference between the effect of dextrose and laevulose is probably due to the retention of the laevulose in the liver, whereas the dextrose is conveyed chiefly to the muscles.

Laevulosuria may occur either (i) because the blood-sugar rises too *Laevulosuria* high, or (ii) because the threshold of the kidney is set at a lower level than usual.

(i) The blood-sugar may be too high because the liver is damaged and is unable to retain the laevulose. This glycosuria was first observed in cases of phosphorus poisoning but may occur in any severe form of toxic liver disease, e.g. chloroform, arsenic, trinitrotoluene, or cinchophen poisoning. A laevulose tolerance test with frequent estimations of the blood-sugar will show a greater rise than 30 mgm. in all cases of severe liver damage (see LIVER DISEASES). The test is of some value in assessing the degree of damage which the liver has suffered in the less severe cases, but it is unnecessary to perform it in the severe cases.

(ii) The normal threshold of the kidney for laevulose is set considerably lower than for dextrose, and glycosuria often occurs when a laevulose tolerance test is performed (Spence and Brett). Laevulosuria sometimes occurs in healthy people, especially if they have been eating plenty of fruit. When the nature of the reducing substance is known it is unnecessary to institute any treatment.

Lactose is a disaccharide and is usually broken down into dextrose *Lactose* and galactose in the stomach and intestines before it is absorbed. Sometimes a little lactose is absorbed into the blood-stream and is then excreted by the kidneys because it cannot be destroyed in the body. When lactose is injected intravenously, over 90 per cent of the amount injected can be recovered in the urine. When over 30 grams of lactose are taken by mouth at one time, a little lactosuria may occur (Folin and Berglund). Lactosuria may occur in lactating women when the milk is *Lactosuria* either very abundant or the baby is not taking its usual amount, and it is always present when lactation is brought to an end suddenly. It is believed that the excess of lactose which is not excreted through the nipples is absorbed into the blood-stream and is consequently excreted by the kidneys. In babies who develop gastro-enteritis lactosuria may occur as a result of the lactose being absorbed unchanged (Grósz). Once the nature of the reducing substance is established the condition does not require any treatment.

Pentoses have only five carbon atoms in their molecules, and they are *Pentoses*

Pentosuria

usually destroyed in the intestines. If they are absorbed into the blood-stream they are excreted by the kidney, as they cannot be destroyed in the body. Pentosuria is liable to occur when an excess of plums, damsons, or cherries is eaten. It also occurs as an inborn error of metabolism (Garrod).

Glycuronates

Glycuronates are excreted in the urine when certain drugs, such as acetanilide (antifebrin), phenazone (antipyrin), amidopyrine (pyramidon), camphor, chloroform, chloral hydrate, morphine, menthol, naphthol, phenol, thymol, or oil of turpentine, are given. These substances are toxic and before being excreted in the urine are combined with glycine as glycuronic acid. Similarly, products of putrefaction, such as indoxyl and skatol, are neutralized before excretion (Harrison).

When the nature of the reducing substance is established, the diagnosis should be confirmed by discontinuing the drug or, in the case of intestinal putrefaction, by trying the effect of purgatives and a low protein diet.

Salicyluric acid

Salicylates are not converted into glycuronates but are synthesized with glycine in the kidney to salicyluric acid. Many patients who are taking large amounts of sodium salicylate excrete sufficient salicyluric acid to cause a definite reduction of cupric sulphate. The excretion ceases as soon as the administration of the drug is stopped.

Homogentisic acid

In alkaptonuria the excretion of homogentisic acid causes a reduction of Benedict's and Fehling's solutions and suggests the presence of sugar. The mistake should not be made, because the addition of the urine at once turns the blue of Benedict's solution to a dark colour and the reduction of the yellow cuprous oxide takes place only slowly. The diagnosis is confirmed by adding a weak solution of ferric chloride drop by drop to the urine. Each drop is followed by a deep purple colour which disappears at once. The addition of the urine to an ammoniacal solution of silver nitrate causes a black precipitate to appear in the cold (Garrod). See also Vol. I, p. 300.

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GOITRE AND OTHER DISEASES OF THE THYROID GLAND

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Reference may also be made to the following titles:

CHAGAS' DISEASE   METABOLISM, BASAL
CRETINISM   MYXOEDEMA
ENOPHTHALMOS AND EXOPHTHALMOS

1.—PATHOLOGY OF THE THYROID GLAND

569.] The thyroid gland regulates the rate of metabolism of the body and is essential to health. In healthy persons the gland is at times observed to increase temporarily in size, notably in young girls at puberty, and it is probable that its activity is altering constantly to meet the requirements of normal life, according to the needs of the person who is in a varying environment and is called upon to perform many functions demanding different expenditures of energy.

Fig. 128.—Normal thyroid gland. (This and Figs. 130 to 133 are from the *British Journal of Surgery*, 1930)

Thyroxine

Thyroxine or a compound of thyroxine is the active principle of the thyroid gland's secretion. The full effects of an injection of thyroxine do not appear for several days; so, possibly, the thyroid gland does not respond to the needs of the body in a sudden emergency but, rather, is responsible for the adjustments that are required over prolonged periods.

Compensation hypertrophy

If in normal animals a sufficiently large proportion of the gland is excised, the remainder enlarges and becomes more vascular, the cellular elements undergo hypertrophy and hyperplasia, and the amount of colloid is diminished. If the gland is inefficient or the demand upon it excessive, it responds in the same way by increased activity accompanied by demonstrable enlargement (see Figs. 128 to 130).

Fig. 129.—Hyperplasia of thyroid gland from a case of diffuse (primary) toxic goitre

A cause of such inefficiency is a deficient supply of iodine, which is an essential constituent of the secretion.

It has been shown both in experimental animals and in man that, *Involution* when the gland has been stimulated to increased activity and has reacted with increased vascularity, hypertrophy and hyperplasia of the cells lining the vesicles, and loss of colloid, it may not return to the normal state of the resting gland when the cause of the increased activity ceases to operate. The process of involution may be faulty, and the whole gland or portions of the gland may then consist of vesicles distended with colloid and lined by flattened epithelium. When a large part of the gland is affected in this way, colloid goitre is produced (see Fig. 131). Colloid goitre is, there-

Fig. 130.—Hyperplasia of thyroid gland from a case of secondary toxic goitre, i.e. superimposed on a diffuse colloid goitre

fore, the result of faulty involution following a phase of increased *Diffuse* activity with hypertrophy and hyperplasia. *colloid goitre*

If the gland is stimulated repeatedly, so that the processes of hypertrophy and hyperplasia and of involution follow each other repeatedly,
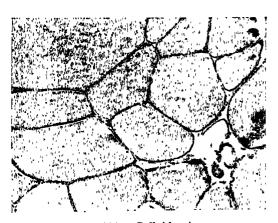
Fig. 131.—Colloid goitre

faulty involution may result in numerous areas of colloid distension separated by areas of normal vesicles. In time the areas of colloid distension by their increasing size compress the gland tissue surrounding them. This, together with newly formed fibrous tissue, causes them to become encapsulated. In the encapsulated areas the walls of the distended vesicles may break down, so that cysts form, haemorrhages may occur, and various forms of degenerative processes develop, including mucoid degeneration and calcification. During the process of involution portions *Nodular* of the gland may fail to return to the resting state and remain *goitre* in the phase of hyperplasia, finally producing encapsulated areas filled with cellular elements. In these ways nodular goitre is produced, the nodules, whether cystic, degenerative or cellular, being the

result of faulty involution following repeated stimulation (see Fig. 132).

Fig. 132.   Nodular goitre

Adenoma

The various conditions of the thyroid gland met with in patients with simple or with toxic goitre can be explained on these general principles of reaction and involution.

The nature of the single encapsulated cellular nodules in which vesicle formation is present but immature is doubtful, and authorities usually speak of them as adenomas (see Fig. 133). It is advisable to consider them as distinct from the involution nodules, for not only is the histological picture different but they may become malignant, and from 80 to 90 per cent of cases of carcinoma of the thyroid gland originate probably in a pre-existing adenoma.

2.–SIMPLE GOITRE

(1)—Definition

570.] Simple goitre may be defined as an enlargement of the thyroid gland without obvious symptoms of deficiency or excess of secretion and not due to malignant disease or inflammation.

(2)—Aetiology

Incidence

It occurs at all ages, but the incidence is highest at puberty. It affects both sexes and, although the distribution between the two sexes varies greatly in different localities, females are in general affected more frequently than males.

Endemicity

It is found in all races of man and in all parts of the world, and in certain areas is so prevalent that it is considered to be

(a)

(b)
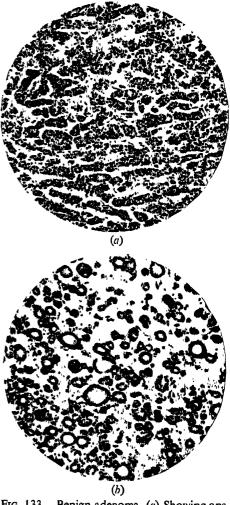
FIG. 133.—Benign adenoma. (a) Showing anastomosing columns of cells forming immature tubules; (b) showing some vesicles containing colloid, some without lumen, others immature

endemic, notably in the Alps, in the basin of the Great Lakes of North America and of the St. Lawrence River, and in certain parts of the Himalayas and of New Zealand. In general, the areas of high endemicity are found in mountainous country or remote from the sea, but there are exceptions. It may be difficult to decide when the incidence is sufficient to justify the term 'endemic'.

McClendon in the United States of America, von Fellenberg in *Iodine* Switzerland, and Hercus, Benson, and Carter in New Zealand demon- *deficiency* strated an inverse relationship between the incidence of endemic goitre and the iodine content of the food and drinking-water. This association of the disease with iodine deficiency has received confirmation in the successful prophylactic use of iodine in these countries. By the administration of iodine the incidence of goitre in school children has been greatly reduced, and its use during pregnancy has successfully prevented goitre in the mother and congenital goitre in the child.

It has, however, not been possible to demonstrate any iodine deficiency in certain endemic areas in Egypt, Sierra Leone, and the Himalayas, and it is not possible to assign a deficient intake of iodine as the cause of sporadic goitre. McCarrison in India showed that polluted water- *Polluted* supplies can produce goitre, and similar evidence has been published *water-supplies* from Egypt. The incidence of enlargement of the thyroid gland at puberty, pregnancy, and the menopause suggests that the sexual *Sexual* functions have an aetiological importance. Heredity is also a factor, *factors* for the incidence in endemic districts is higher among the offspring of *Heredity* parents both of whom are goitrous and is greatest when several generations of ancestors have been goitrous. The onset or an aggravation is *Infections* frequently observed in association with infective diseases, such as acute tonsillitis and influenza.

Animal experiments suggest that other factors may be found in un- *Diet* suitable diets and in general unhygienic conditions, and the recently discovered thyrotropic hormone in the anterior lobe of the pituitary, *Pituitary* which on injection into guinea-pigs, rats, and rabbits produces hypertrophy and hyperplasia of the thyroid gland, may be an important clue to the causation of the disease. All these forms of experimental goitre can, however, be prevented by iodine.

The cause of the disease is generally regarded as a diminished capacity of the gland to meet the demands made upon it. The deficiency may be inborn or hereditary, or it may be the result of a deficient intake of iodine. On the other hand, it may be the result of an excessive demand upon the gland by such conditions as infective diseases, unhygienic conditions, or excessive stimulus from the sex glands. In endemic goitre a combination of factors is responsible for the incidence of the disease, and, although it is difficult in any case of sporadic goitre to decide on the factor or factors concerned, it is probable that the aetiological principles are the same.

(3)—Pathology

In the early stages of the disease the gland is believed to pass through the stage of hypertrophy and hyperplasia, but this, being long past before operation is required, is seldom seen in the glands removed from patients. It is found in the glands of children and in congenital goitres in areas of high endemicity. The puberty goitre occurring in areas of low endemicity and in sporadic cases is usually of the diffuse colloid type, but in older patients in all countries the thyroid gland of simple goitre is usually found to be nodular. The nodules may be colloid, cystic, or cellular, or show various conditions of degeneration; and nodules of several different varieties may be present in one gland. Various degrees of fibrosis are always present in the nodular glands.

Simple goitres may be classified as (i) diffuse, (*a*) hypertrophic and hyperplastic, (*b*) colloid; and (ii) nodular, (*a*) multiple involution nodules, (*b*) single (adenoma).

(4)—Clinical Picture

Hypo-thyroidism

Hyper-thyroidism

As might be expected from the evidence that simple goitre is indicative of a deficient thyroid gland, mild symptoms of hypothyroidism are found in many instances, but there are also patients who at the age of puberty present symptoms suggestive of a slight degree of hyper-thyroidism. In most cases, however, there are no symptoms; if symptoms arise they are due to the mechanical effects of the enlarged gland,

Compression effects

which may cause pressure on the trachea or oesophagus. Colloid goitres are softer than the nodular goitres and, unless very greatly enlarged, do not commonly compress these structures. In all forms the lateral lobes may extend backwards and inwards, forming an en-circling mass that compresses the trachea laterally. In many instances, particularly in the nodular goitres, the masses extend downwards behind the sternum and may then compress the trachea antero-posteriorly. Irregular nodular masses in the upper mediastinum may push the trachea to one side, compressing it laterally.

When the trachea is compressed, shortness of breath on exertion and a feeling of constriction are noted by the patient and, if there is much compression, this may cause obvious obstruction to respiration. Dangerous obstruction may arise rapidly from haemorrhage into the substance of the goitre, and increasing distress, probably due to increase in the size of the goitre, is seen in acute infections of the upper respiratory passages. Pressure on the trachea is accompanied by chronic cough and sometimes by stridor.

On veins

Pressure on veins is usually the result of extension downwards into the upper mediastinum; other structures, such as the oesophagus, the apices of the lungs and thoracic duct, are rarely compressed.

(5)—Course and Prognosis

The prognosis in simple goitre is so variable that it is scarcely justifiable to draw generalizations. Undoubtedly many girls show evidence of

enlargement of the gland for the first time at puberty; this enlargement frequently disappears in adult life, and there is not any further evidence of disturbance of the thyroid gland. On the other hand, simple goitre arising before puberty is likely to persist. Established goitre often becomes toxic at or about the menopause, but the frequency with which this occurs seems to vary greatly in different countries. A patient with goitre should always be guarded and carefully guided through pregnancies and acute infections, for at such times exacerbations are liable to occur or toxic symptoms to develop for the first time. When the goitre is substernal or intrathoracic there is always danger of pressure on the trachea.

The prognosis following surgical treatment is good, but the condition occasionally recurs and requires further operative measures; and symptoms of hypothyroidism occasionally arise necessitating the administration of thyroid gland.

(6)—Treatment

In endemic areas the administration of iodine to children and to *Prophylaxis* pregnant mothers has greatly reduced the incidence of simple goitre. In such areas the use of iodized salt is convenient and effective, sodium *Iodized salt* iodide or potassium iodide being added to table salt in the proportion of 1 in 200,000. A daily dose of 0·1 mgm. ($\frac{1}{600}$ grain) of iodide is generally regarded as suitable. Such prophylactic measures do not entirely prevent goitre even in children, nor do they prevent its occurrence later in life, and prophylactic measures are not practicable for sporadic goitre.

Once a simple goitre has appeared, general measures to relieve physio- *Medical* logical stress and to improve the general hygiene of the patient should *treatment* be instituted. Chronic infections should be cleared up and overwork at school avoided. In the early stages iodine may be effective, but, when *Iodine* involution has taken place and a colloid goitre has resulted, it is doubtful if iodine can produce much reduction in size. Iodine is ineffective when nodulation and fibrosis have taken place. Even in colloid and nodular goitres further hyperplastic reactions occur from time to time, as in pregnancy or with acute infections, and iodine can then bring about a reduction in size of the gland. In all cases, therefore, iodine should be tried first. One grain of iodine daily is a suitable dose, and this is contained in about one and a half grains of potassium iodide, and in about ten minims of Lugol's solution or of simple solution of iodine (B.P. 1932).

There is some evidence that the injudicious use of iodine in large doses *Danger of* may cause a patient with simple goitre to develop symptoms of toxic *iodine* goitre, but this danger seems to be limited to certain endemic areas. There is no clear evidence that this occurs among the cases of sporadic goitre found in the British Isles.

If iodine fails to produce any reduction in size at the end of three or *Thyroid* four weeks, thyroid should be given and, although this also is more

efficacious in the early stages, will sometimes cause a dramatic subsidence of a diffuse or even a nodular goitre. Success is most likely to be met with when symptoms of hypothyroidism are present. The treatment must as a rule be continued indefinitely, but great care must be exercised; when, as is sometimes the case, tachycardia results with quite small doses, it may be extremely difficult to find a dose that does not produce

Dosage symptoms of hyperthyroidism. It is best to begin with a dose of half a grain daily of the dried thyroid gland (thyroid B.P. 1932) and to increase the dose at intervals of ten days up to three or five grains daily, if no undue tachycardia or other symptoms of overdosage appear. The patient should be kept under close observation, and smaller initial doses are advisable for young children. Success or failure with iodine and with thyroid probably depends on the aetiology of the condition and the state of the gland, and the aetiology is uncertain, especially in the sporadic forms.

Surgical treatment Surgical treatment should not be employed till it is found that neither iodine nor thyroid is efficacious. The aims of surgical treatment are the relief of pressure and the removal of an unsightly swelling. Surgery may

Indications be urgently required in those rare cases in which tracheal obstruction develops rapidly and there is no time in which to try the effects of iodine and of thyroid. In general, surgical treatment is indicated earlier in those cases that show from time to time mild symptoms of hyperthyroidism, and it is always indicated in those in which the goitre is intrathoracic or substernal. It should be delayed as long as possible when symptoms of hypothyroidism are present. Even in the absence of any symptoms of ill health or of pressure, the existence of the swelling in the neck may so prey on the mind of the patient, or be such a drawback to the chances of employment or of marriage, that surgical treatment is indicated.

Adenoma The single encapsulated cellular nodule—or adenoma—should be removed as soon as pressure symptoms arise or if its presence is in any way disturbing to the patient, for the surgical procedure is simple, and

Other forms there is a possibility of malignant changes supervening. Surgical treatment for diffuse colloid goitre or for simple nodular goitre should be so carried out that essential structures are protected, a symmetrical neck is left, and the resulting scar is scarcely more conspicuous than a normal crease in the neck.

3.–TOXIC GOITRE

(1)—Definition

571.] The term toxic goitre is used to include all forms of thyroid disease in which there are signs of hyperthyroidism. Arguments have been brought forward for an abnormal secretion of the gland in toxic goitre,

Dysthyroid-ism and the term dysthyroidism has been proposed; but there is no clear evidence that the gland ever produces an active secretion other than thyroxine, and so the dysthyroidism is hypothetical. Some patients appear to present signs of excessive secretion and of diminished activity

of the thyroid gland at the same time, and for this and other reasons it is difficult to accept a simple hyperthyroidism as the explanation of the condition. In the present state of knowledge, therefore, the terms toxic goitre, thyrotoxicosis, or thyroid intoxication are preferred to the more definite terms hyperthyroidism and dysthyroidism. All cases, however, show signs of excessive activity of the gland.

Toxic goitre includes the conditions known as exophthalmic goitre, *Variety of* Graves's disease, Basedow's disease, toxic adenoma, and nodular toxic *forms* goitre; and the inclusion of these under one title is based on the belief that the essential abnormality is, in the light of present knowledge, the same in each, and that it is often impossible to draw a distinction between them. It is a common practice to designate as primary toxic *Primary toxic* goitre those cases in which the symptoms of thyroid intoxication arise *goitre* in a patient who previously has not shown evidence of thyroid disease, and as secondary toxic goitre those in which the symptoms develop in *Secondary* a patient who has had a simple goitre for some time previously. This *toxic goitre* distinction has a value in describing cases, but it is a difficult one to make with confidence in all instances. It has probably no value from the point of view of aetiology and no constant value in deciding upon the treatment to be adopted, and is not an essential distinction. As a guide to treatment and prognosis it is more important to distinguish the cases in which the thyroid disturbance is the important factor in the ill health of the patient from those in which it is but a part of a more general disorder.

As evidence accumulates of the interrelations of the endocrine glands *Endocrine* and of the influence that abnormalities of these glands have on the *glands* thyroid, it may become possible to draw a distinction between toxic goitre due to a disturbance primarily of the thyroid and toxic goitre secondary to disturbances of other organs or glands, such as the anterior lobe of the pituitary.

Symptoms of thyroid intoxication are occasionally reported in cases of malignant disease and of inflammation of the thyroid gland (thyroiditis), but in these the disease processes in the gland are more important than the disturbance of function and will be discussed under the appropriate headings.

(2)—Aetiology

Toxic goitre is found in all parts of the world and, so far as is known, *Geographical* no race is exempt. In the southern states of North America the incidence *incidence* appears to be higher in the white population than in the negroes. The incidence is high in some areas of high endemicity of simple goitre, but this parallelism is not seen in the mountainous areas of Switzerland or in the Himalayas, for toxic goitre is not more prevalent in the districts where the incidence of simple goitre is especially high than in neighbouring areas where it is lower. In Great Britain a similarity in the distribution of the two diseases can be demonstrated.

No age is exempt; the disease has been recorded in the new-born and *Age incidence*

in the aged, but the frequency rises rapidly after puberty to its height in the third decade. The incidence rises again about the time of the menopause, and, when the disease occurs at that time or later in life, there is usually evidence of the presence of simple nodular goitre for some years previously.

Sex incidence   All observers are agreed that the disease is commoner in females than in males. The relative frequency in the two sexes recorded in the literature varies between fifteen females to one male and three females to one male. The latter figures were for patients over fifty years of age.

Causation   The cause of toxic goitre is not known, and it is probable that several factors contribute to its production, and that these factors differ from case to case. Certain events are so frequently associated with the onset or with exacerbations and relapses that they have an aetiological significance.

Infections   The onset of the disease often follows an attack of influenza or of diphtheria. Acute tonsillitis is important, especially as the cause of relapses, and in the chronic forms of toxic goitre chronic infections of the tonsils or of the nasal sinuses should be treated, since acute exacerbations of these infections may determine dangerous relapses of the toxic goitre. It is also probable that chronic infections of the tonsils and sinuses contribute to chronicity of the thyroid disease. Typhoid, pneumonia, and rheumatic fever have been quoted as exciting causes.

Sex life   The incidence of the disease is high in early adolescence and about the time of the menopause. An increase in the severity of the symptoms is often observed during menstruation. Some patients date the onset to the puerperium. The disease seems to decrease the chances of pregnancy, but during pregnancy the symptoms often subside. These observations and the high incidence in females in comparison with males point to a real but so far undefined aetiological factor associated with the functions of the sex organs.

Emotional shocks and stresses   Numerous cases are recorded in which the onset of the disease is associated with sudden shocks, such as air raids, sudden deaths of relatives, or the sight of fatal accidents, but long-continued mental and emotional stresses are more usual as exciting causes. The worry and fatigues associated with the nursing of a near relative through a long illness and the silent struggle with financial difficulties are frequent factors. Perhaps the most potent forms of mental disturbances are those associated with the emotions, the unhappy marriage with its continued irritations and inhibitions, the broken engagement, and the fear of undesired pregnancy.

Constitution   Such events, however, occur in the lives of many who do not develop toxic goitre, and arguments for an underlying constitutional factor have been brought forward by many writers. The disease occurs sufficiently often in two or more members of a family, such as mother and daughter, two sisters, or aunt and niece, that a familial and inherited constitutional factor must be considered.

Attention has been drawn to the similarity of many of the symptoms

of toxic goitre to the phenomena that can be produced experimentally by stimulation of the sympathetic or the parasympathetic fibres of the autonomic nervous system, and it has been suggested that the con- *Nervous* stitutional factor is a disturbance of the normal balance between these *imbalance* two parts of the autonomic nervous system. It is tempting to speak of a constitutional type that is liable to develop toxic goitre, but, until this can be more clearly defined, it must be regarded as hypothetical.

As a result of animal experiments and of clinical and post-mortem observations on patients, the relations between the thyroid gland and the adrenal glands and between the thyroid gland and the anterior lobe of *Endocrine* the pituitary are being defined. From the anterior lobe of the pituitary *glands* can be isolated a thyrotropic substance which produces in animals a condition closely resembling that of toxic goitre, but it is not yet possible to assess the aetiological importance of disturbances of this gland.

(3)—Pathology

The most characteristic pathological condition is a moderately enlarged gland showing vascular engorgement and hypertrophy and hyperplasia *Hypertrophy* of the cells lining the vesicles, which are almost empty of colloid and *and* filled by the cellular elements (see Fig. 129). This appearance is character- *hyperplasia* istic of the severely toxic case with exophthalmos in a young female before the administration of iodine, but it is not so often seen now that the use of iodine in treatment has become wide-spread.

Treatment by iodine causes involutionary changes, the storage of *Involution* colloid, and a return towards the appearance seen in the normal or resting gland. There are often collections of lymphocytes in the inter- stitial tissues.

The pathological condition of the thyroid gland is found to vary *Varieties* considerably from case to case, and there is none which can be regarded as distinctive of toxic goitre. The gland may be very greatly enlarged or may be small and fibrotic. It may be diffusely hyperplastic or resemble that of diffuse colloid goitre. It may be nodular, and the nodules may be cellular or colloid or show degenerative changes, cystic, haemorrhagic or mucoid, or be calcified. It may extend substernally or be situated in the mediastinum. The degree of abnormality in the macroscopic and microscopic appearances of the gland cannot always be correlated with the clinical severity of the disease.

Characteristic changes are not found in the other organs of the body. *Changes* The ovaries, pituitary, adrenals, pancreas, and parathyroid glands often *elsewhere* show changes, either atrophic or hypertrophic, but none is constant. Abnormalities in the thymus are more often recorded. The liver is said to be poor in glycogen, and any changes found in the kidneys of fatal cases are probably due to intercurrent inflammations or degenerations.

The heart may show slight or moderate dilatation and hypertrophy, *Heart* but any marked changes are due to factors other than the thyroid disease, such as arteriosclerosis, hypertension, or rheumatic valvular lesions. In spite of the striking clinical disturbances of the heart in this disease it is

difficult to find any abnormality of the muscle-fibres of the heart after death. As death from toxic goitre is commonly associated with congestive heart failure or acute respiratory infection, the pathological changes due to these conditions are found.

Nervous system

Histological examination of the nervous system, especially the involuntary nervous system, has failed to demonstrate any constant structural abnormality.

(4)—Clinical Picture

The clinical picture varies greatly. In general most of the signs and symptoms are present in the younger patients, but in the older patients any of them may be absent, and such disturbances as auricular fibrillation and congestive heart failure, which are rare in the younger patients, may dominate the clinical picture. Very rarely the enlargement of the thyroid gland may be difficult to determine without special methods of examination. The disease may be severe and acute, the height of severity being reached in a few days from the onset, or it may be extremely mild and chronic, such symptoms as are present being considered part of the temperament and constitution of the patient.

The extreme variability of the clinical picture is perhaps to be expected, for the exciting causes differ from case to case and there are certainly other causes not yet defined; the disease may arise in a patient who has had a simple goitre for many years and in whom the gland is structurally abnormal, or it may arise in a patient whose gland has been hitherto healthy; and it may arise in a young patient whose organs can withstand the disease without evidence of functional failure, or in an elderly patient whose heart or nervous system or other organs cannot stand even mild degrees of thyroid intoxication without functional failure. If the variations in the stimulus to the gland, in the capacity of the gland to react, and in the ability of the organs to withstand the hyperthyroidism are considered, the extreme variations in the clinical picture can be comprehended.

'Thyroid crisis'

The severest and most acute form of the condition, termed 'thyroid crisis', is less often seen, whether arising spontaneously or immediately following thyroidectomy, since the use of iodine in treatment was reestablished by Plummer and Boothby in 1923.

The size and shape of the gland can be ascertained by inspecting the neck in front and from the side when the patient swallows with chin slightly raised and by palpating from behind, passing both hands forward and delimiting the isthmus and the lobes with the finger-tips.

Thyroid enlargement

In chronic cases or when toxic goitre arises in a patient who has had a diffuse colloid or a simple nodular goitre previously, the gland may be greatly enlarged and irregular, but more characteristically the enlargement is slight or moderate and involves the gland diffusely. Sometimes the enlargement seems to affect the isthmus, one lobe, or a portion of a lobe rather more than the rest of the gland, but even then the whole of the gland is involved. The surface may not be quite smooth, slight

palpable irregularities being due to the exaggeration of the normal lobulation. In consistence it is firm but not hard and is not tender. When the disease has lasted for some time, irregularities become more pronounced, and the gland becomes harder. such changes occurring earlier when iodine has been given.

In the severer cases the excessive vascularity of the gland can be recognized by a palpable thrill and a systolic murmur, but these signs disappear rapidly when iodine is given. Murmurs may, however, be heard over very large glands and especially over nodular glands in the absence of toxicity.

The presence of a goitre may be noticed by the patient, who may complain of a sensation of fullness in the neck, but in the absence of previous thyroid disease the enlargement is usually first observed by a relative or by the doctor to whom the patient has applied because of other symptoms.

In rare instances the thyroid gland cannot be seen or palpated in the neck, but on X-ray examination the enlarged gland is found behind the manubrium sterni.

Exophthalmos is not always present. It may be absent in the younger *Exophthalmos* patients and is frequently absent in the more elderly. If present in the latter it is more often slight in degree. It is usually bilateral but may be more pronounced on one side, and it is occasionally unilateral. It may be so extreme that dislocation of the eyeball results, and conjunctivitis is commonly an accompaniment of the more severe grades. It may vary in degree from day to day and may, rarely, arise in the course of a few hours and as rapidly subside but, when established for any length of time, is the most persistent sign of the disease, sometimes remaining when recovery is otherwise complete.

The mechanism of its production is unknown. The rapidity with which *Mechanism* it can arise or become aggravated and its prompt disappearance after death suggest that it is caused by stimuli through the sympathetic nervous system to the unstriated muscle-fibres of the orbit. Venous engorgement and oedema, possibly the result of contraction of these muscles, may be added factors, and in cases in which it has persisted for many years there is evidence of an increase in the fat content of the orbit. The observation that the injection of extracts of the anterior lobe of the pituitary can produce exophthalmos in experimental animals and in man and the difficulty in producing it by the administration of thyroxine point to the association of this phenomenon with some disturbance of the endocrine or nervous system in addition to hyperthyroidism.

Even when proptosis of the eyeball cannot be demonstrated, the eyes *Retraction of* often appear to stare abnormally. This is due to retraction of the upper *the upper lid* lid, which may be so slight that a previous acquaintance with the patient is necessary for its recognition. In combination with exophthalmos it may prevent the closure of the lids and the cleaning of the conjunctival surface. It is a more constant sign than exophthalmos and is probably

due to contraction of the unstriped muscle-fibres in the upper lid described by Müller.

Other eye signs

Infrequency of blinking and a glistening of the conjunctiva due to increased lacrimal secretion also contribute to the characteristic appearance of the eyes. Not uncommonly a sensation described by patients as a gritty feeling at the back of the eyeball is present.

Many other signs associated with the eyes have been described, but the only ones that deserve mention for their value in diagnosis are the lack of wrinkling of the forehead when the patient looks up (Joffroy's sign), the lagging of the upper lid when the eyes are slowly turned downwards (von Graefe's sign), and the difficulty of convergence on looking at a near object (Möbius' sign).

Ophthalmo-plegia

External ophthalmoplegia affecting any one or all of the external muscles of the eyeball is rare; it usually accompanies exophthalmos and may similarly prove to be associated with some disturbance of the endocrine or nervous systems other than hyperthyroidism.

Cardio-vascular disturbances

Palpitation

The cardiovascular system is characteristically affected. Palpitation may be the earliest complaint. In severe cases it may be present even at rest and may produce a sensation as if the heart would break through the chest wall. In the milder cases it is absent at rest but is noticed on the slightest exertion and accompanying any emotion, whether pleasurable or otherwise. The sensation of throbbing may be felt by the patient in the vessels of the neck as well as in the chest. Pain, as in angina pectoris, is rare.

Hot flushes

Hot flushes are usual in the younger patients but may be absent in the older and are felt in the neck, face, and upper thorax especially. They are usually accompanied by a visible flush and result from emotional disturbances. Independently of the sensation of sudden flushes a general feeling of uncomfortable heat throughout the whole body is common and comes and goes without obvious cause.

Cardiac impulse

Examination of the heart shows that the cardiac impulse is exaggerated and its character indicates a vigorous and rapid action, as in a healthy person after extreme physical exertion. The impulse may be felt all over the praecordia, and the apical impulse may be so diffuse that it is felt outside the normal position, and enlargement of the heart is suspected, even when on radiological examination it is seen to be normal in size.

Cardiac enlargement

In severe cases or when the rapid action has persisted for long the heart is enlarged, but when great enlargement is found there is usually some other responsible factor, such as previous rheumatic carditis or hypertension, in addition to the thyroid disease.

Cardiac sounds

The sounds are loud and sharp, but systolic murmurs at the apex and base are usual, and in severe or long-standing cases the first sound may become blurred. If other endocardial murmurs are present they are due to some other disease. It is not uncommon to hear over the inner end of the second and third left intercostal spaces a scratching sound in systole, resembling pericardial friction and due probably to change in the tissues overlying the conus of the right ventricle. Over the vessels

of the neck and the thyroid gland a low-pitched murmur, continuous, but with systolic accentuation, may be heard.

The rate of the heart is characteristically rapid and varies with the *Tachycardia* severity of the disease; it may reach 180 or more per minute, but more commonly rates of 100 to 120 per minute are found. The rate is remarkably constant throughout the day when the patient is at rest in bed, but in mild cases or during remissions, even when a normal rate occurs with the patient at rest, it rises readily to 100 or even higher on slight exertion or excitement.

The heart's action is usually regular; but, if the disease is very severe *Cardiac* in the younger patients and even if only mild in the older, auricular *action* fibrillation is likely to arise. With the onset of auricular fibrillation *Auricular* congestive heart failure results, and life is endangered or the patient *fibrillation* condemned to chronic invalidism. This constitutes one of the special dangers of toxic goitre. The irregularity is often not recognized, for the ventricular contractions may not be so obviously irregular in rate and force as in auricular fibrillation due to other conditions.

Other irregularities of the heart are rare, but extrasystoles and auricular *Other* flutter occur, usually shortly before the onset of auricular fibrillation. *irregularities* Paroxysms of auricular fibrillation are common before the irregularity becomes established.

The radial artery is soft, and the pulse has a quick rise and fall with a *Pulse* large expansion with each beat. These characteristics are in keeping with the blood-pressure, for the systolic pressure is usually raised, the diastolic normal, and the pulse-pressure increased. Systolic pressures of 140 to 160 mm.Hg and diastolic of 80 mm. are usual in cases of moderate severity.

The most constant and one of the earliest symptoms noticed by the *Muscular* patient is a general weakness of voluntary muscles, with a rapid onset *weakness* of fatigue on physical exertion. There are few patients who do not experience this at some time in the course of the disease, and it produces an irritating sensation of inefficiency.

A fine tremor of the outstretched fingers is usual but sometimes absent *Tremor* in the older patients. The tremor may be seen in the tongue and lips, and in severe cases it may be felt in all the muscles of the body. Usually it is slightly irregular but in some cases is grossly irregular and less fine.

In addition to the tremor twitching of the muscles may be present and *Twitching of* can be appreciated by palpating the tendons in the region of the wrist *muscles* when feeling the radial pulse.

In many patients there is also a restlessness, so that they cannot sit *Restlessness* or lie still but are continually altering their posture and the position of their limbs. In severe cases this gives rise to redness of the skin over the elbows and knees from continual rubbing against the bed-clothes.

Mental unrest is often the earliest manifestation observed by the *Mental state* relatives. Excessive mental energy with optimism and exaggerated emotional reaction, irritability and intolerance of the behaviour of those around, followed by depression and bursts of sulky anger, sometimes

occur. The mental state is extremely trying to other members of the household and causes them in turn to be irritable and impatient, so that they aggravate the mental condition of the patient. Acute mental disease, usually maniacal but sometimes depressive in type, is rare but constitutes one of the serious complications.

Loss of weight

The weight of the patient and the direction and rate of change in weight are valuable guides to the severity of the disease and to its activity. So long as loss of body-weight continues the disease is active, and cessation of loss and beginning of gain are indications of remission. Weighing the patient at weekly intervals is perhaps the best clinical method of measuring the activity of the process. In severe cases the loss of weight is rapid and striking, and many pounds of weight are lost in the course of a few months, the patient being reduced to an appearance of skin and bones. The basal metabolic rate is discussed on page 617.

Patients who do not lose weight

Some patients with moderate or slight enlargement of the thyroid gland, mental and emotional disturbances, tachycardia on exertion or excitement, and minimal or no eye signs, do not lose weight and are sometimes plump and rounded in form with no loss of subcutaneous fat. They often give a history of prolonged neurasthenic disturbances, nervous breakdowns, and emotional instability previous to the onset of thyroid enlargement and constitute an important group, because treatment on the usual lines for toxic goitre does not restore them to efficiency. Thyroidectomy may be followed by mental depression without alleviation of the emotional and neurasthenic symptoms. It is probable that the thyroid disturbance is but an incident in a general disorder of the nervous system.

A similar group presents exophthalmos and other eye signs, no loss of weight, little or no enlargement of the thyroid gland, and no other manifestations of thyroid intoxication. In them also it is probable that the thyroid gland is playing a subsidiary part in the ill health of the patient and that the primary disturbance has yet to be discovered.

Other symptoms

Temperature

Most systems and organs of the body may be disturbed at times and produce symptoms of varying severity. Slight and irregular rises of temperature are common but not clearly related to the severity of the disease, although in the acute crises and in the critical conditions that may occur immediately after the operation of thyroidectomy temperatures of 103° F. or higher are usual. A daily elevation of the temperature to 99° F. or over is not indicative of a complicating infection.

Dyspnoea

Dyspnoea is usual on exertion and may in severe cases be present at rest. When the thyroid is large and nodular or when it has become hard as the result of the administration of iodine, a sense of constriction to respiration may be experienced. With substernal goitres actual displacement and compression of the trachea may be present. With the development of congestive heart failure the dyspnoea may be very great.

Cough

Cough is usual in the severe cases and may be due to irritation and congestion of the tracheal mucous membrane caused by pressure of the goitre from without.

In the acute crises of the disease vomiting may be frequent, but apart *Appetite*
from these it is rare. As a rule the appetite is unusually good; but among
the older patients and when the disease has continued for some years
there are a few cases in which anorexia is present. The usual periods of
physical and mental energy, as if the patient were being driven from
within, are absent in these cases, and their appearance and attitude
suggest that they are exhausted or 'burnt out'. They form a group that
presents many difficulties in treatment.

Achlorhydria is found, but the incidence has not been shown to be *Achlorhydria*
higher than in the general run of hospital patients, nor is it associated
especially with the cases in which anorexia is present.

Constipation is rare; diarrhoea is more often present but is temporary, *Diarrhoea*
and, although a mild degree of abdominal unrest is common, the
intestinal functions are rarely disturbed to any great extent.

The skin is peculiarly soft, moist, and warm in most patients; the *Skin*
sudden flushes and the erythema in the region of the elbows and knees
have already been described (see pp. 612 and 613). Itching is not
uncommon; when present it is peculiarly distressing and may result in
constant rubbing and scratching with excoriation of the surface.

Excessive sweating is a common complaint, and the condition of the *Sweating*
skin and cardiovascular system, with the increased superficial circula-
tion, is associated with a marked dislike of hot weather and warm
stuffy rooms and a preference for cold weather and for ventilation.
This characteristic condition of the skin is not always found, but a
harsh dry scaly skin is rare and usually antedates the onset of the disease.

Symmetrical localized swellings of the subcutaneous tissues, which do *'Localized*
not pit on pressure, occurring usually on the anterior and lateral aspects *myxoedema'*
of the lower two-thirds of the legs below the knees are rare. This has
been described as 'localized myxoedema' but accompanies toxic goitre
and disappears slowly during recovery after thyroidectomy.

Anaemia is not a feature of the disease, but a mild grade of hypo- *Anaemia*
chromic anaemia is frequent and disappears with remission or recovery.

Disturbances of menstruation are common. Irregularity and diminished *Menstruation*
loss are usual, and complete cessation of menstruation for several
months may occur. These disturbances are not accurately related to the
severity of the disease but are more frequent in the severe cases. Women
with toxic goitre are less likely to become pregnant than healthy women,
and sexual desire is commonly reduced. In some cases, however, sexual
desire is enhanced.

The frequent association of acute tonsillitis with the onset or with *Tonsillitis*
relapses has already been referred to, and chronic tonsillar sepsis is
probably related to the maintenance of activity, but even when no acute
or chronic sepsis can be demonstrated the tonsils and other collections
of adenoid tissue in the pharynx are often seen to be swollen and en-
gorged, especially in the younger patients. This condition disappears
with successful treatment of the thyroid disease.

Glycosuria is not uncommon but is seldom persistent, disappears with *Glycosuria*

rest and partial recovery, and is accompanied by a normal blood-sugar level when the patient is fasting. True diabetes mellitus occurs, but there is no clear evidence that its frequency is higher in toxic goitre than in other disease.

(5)—Course and Prognosis

The disease may run a short course with recovery after a few months, but this is rare. If the onset is associated with a definite causal factor, such as an acute infection or emotional stress, early and complete recovery may occur. Usually the course of the disease is long, repeated relapses of varying severity alternating with periods of remission of varying duration. A remission may last for years and the disease be mild and chronic; but, once the disease is established, complete recovery is unusual. So long as the disease is present there is the possibility of a relapse sufficiently serious to cause death, and when the disease is chronic there is the likelihood that auricular fibrillation will develop about the time of the menopause or in the later years of life with invalidism or death from congestive heart failure.

The course must depend to some extent on the circumstances of the patient. If a quiet restful guarded life can be assured, the chances of a serious relapse are less than when the patient must face the necessity of earning a living or of bringing up a large family.

Effect of operation
The course and prognosis are greatly altered by the operation of subtotal thyroidectomy. Cessation of activity of the disease and recovery usually result and, even if the effect is not so good as this, danger of a serious and fatal relapse is removed, and serious complications, such as auricular fibrillation, are rendered improbable.

The disease rarely recurs after subtotal thyroidectomy, but the underlying constitutional abnormality is still present, and operative treatment must be regarded as an incident in the management, the patient requiring care and guidance throughout life, avoiding mental and emotional strain and excessive physical exertion. In the event of acute infection steps must be taken to ensure a prolonged convalescence and thorough recovery.

Children
The course and prognosis in childhood are similar, but at the time of puberty, when the thyroid and other glands are especially going through a process of readjustment, the course is more difficult to foresee, and, if possible, thyroidectomy should be delayed until the effect of adolescence can be gauged.

Elderly patients
In the later years of life the disease is seldom severe, but the patient's organs are less able to stand the strain, and functional failure is seen, even though the degree of toxicity may be slight. Mental disturbances and auricular fibrillation are to be expected, and thyroidectomy should be performed early to prevent these complications.

Pregnancy
During pregnancy a remission of activity is often seen, but a relapse is common in the puerperium, and the condition of the patient is more serious than before the pregnancy. Artificial termination of the preg-

nancy, except in the first two or three months when it does not appear
to produce any ill effects, may cause a serious aggravation of the
disease and is seldom advisable. If the condition of the patient is such
that the continuance of the pregnancy to its normal termination is
improbable, two courses are open—thyroidectomy allowing the preg-
nancy to proceed to term or termination of the pregnancy—and each
case must be judged on its merits.

(6)—Diagnosis

The diagnosis does not present difficulties when the symptoms and
signs are characteristically developed. Difficulties arise when the thyroid
gland is not obviously enlarged and typical eye signs are absent.

Anxiety states present the greatest difficulty, as muscular weakness, *Anxiety*
tremors, tachycardia, vasomotor instability, and mental agitation may *states*
all be present. In toxic goitre the peculiar staring appearance of the
eyes will usually also be present, and careful examination of the thyroid
gland will disclose enlargement. It is possible that a disturbance in the
functional activity of the thyroid gland is present in anxiety states, for
undoubted signs of toxic goitre may be found in patients who have
suffered from nervous and mental instability and had neurasthenia or
anxiety disturbances for years before the signs of toxic goitre appear.
It is important to differentiate these cases from those in which the
condition is primarily due to the thyroid gland, for treatment by
thyroidectomy not only fails to improve them but may even make the
condition worse. A careful history and a study of the conditions of the
patient's business and home and of personal and especially marital
relations are necessary to decide whether the case is primarily one of
toxic goitre or whether the thyroid disturbance is an incident and a
comparatively unimportant accompaniment of a long-continued mental
and nervous disorder.

Chronic infections, such as pulmonary tuberculosis or chronic pyelitis *Chronic*
due to *Bacillus coli*, with muscular weakness, tachycardia, and a low- *infections*
grade irregular pyrexia will rarely be mistaken for toxic goitre.

In elderly people with auricular fibrillation due to toxic goitre eye
signs, tremor, nervousness, and loss of weight may all be absent and
the signs of congestive heart failure so obvious that the thyroid origin
of the condition may be missed unless the thyroid gland is carefully
examined. If no other disease process can be found as a cause of the
cardiac irregularity, toxic goitre should be considered, and the evidence
will usually be forthcoming.

The basal metabolic rate is raised in toxic goitre and is a useful *Basal*
measurement of its severity. Repeated estimations of the rate provide *metabolic*
an indication of progress, of a relapse or a remission, but this measure- *rate*
ment is not often of value in the diagnosis of the condition when the
methods of clinical examination fail. The difficulties of conducting the
test under basal conditions and the wide range of values obtainable
in nervous and ill patients not suffering from toxic goitre render the test

of little value in differentiating between mild thyroid toxicity and an anxiety state, or between the mild toxicity that may be responsible for auricular fibrillation in an elderly patient and the elevation of metabolism that occurs in congestive heart failure. Means (1933) considers that estimation of the basal metabolism before and after the administration of iodine can help in difficult cases. (See METABOLISM, BASAL.)

Leucocytes   The total leucocyte count is usually normal, but the lymphocytes are said to be slightly increased and the polymorphonuclear cells diminished. The characteristic changes are slight and by no means constant, and the leucocyte count is liable to slight variations from so many causes that this method of differentiation is not of practical value.

For the purposes of treatment and prognosis it is not sufficient to diagnose toxic goitre. A decision must be made whether the patient's ill health is due mainly to the thyroid disturbance or is but part of a general and long-standing disorder, and whether the disease is in the stage of active relapse or of remission. These questions can be decided only by a careful history of the patient's activities and efficiency in the past, by a study of the relations of the patient to the personalities at home and at work, and by observation of the patient in a hospital or nursing home.

(7)—Treatment

Medical   Since the cause of toxic goitre is not known, specific treatment directed to the cause is not available, and even surgical treatment by subtotal thyroidectomy must be regarded as symptomatic. Whether surgical treatment is to be employed or not, the aim of the physician is to bring about a remission of the disease, for the risks of operation are much less during that phase.

Rest   The most valuable method of treatment is rest, which must be physiological rest and rest for the mind as well as for the body. When the conditions of the patient's home have been studied, it will usually be found that irritations have occurred and incompatibilities exaggerated as a result of the disease, or it may even be suspected that strained relations between husband and wife or parent and child have a causal connexion with the condition, and that transference to a nursing home or hospital is advisable. Only in the milder cases can treatment be efficiently carried out in the patient's home. All sources of worry at home or in business should be sought for and disclosed and if possible removed. The surroundings should be quiet and cheerful and the nurses and attendants congenial to the patient. At first strict rest in bed should be enforced, while sources of infection are sought for and the severity of the condition is judged. After a few days a considerable improvement will be seen, except in the more severe cases, and in favourable cases this improvement continues, the tachycardia subsides, the nervousness disappears, the patient gains weight, and a remission sets in. In many, however, in spite of a considerable initial improvement, tachycardia and loss of weight persist.

The use of special diets is not clearly indicated. The metabolic rate is *Diet* raised, and the patients are usually hungry, so that a generous, well proportioned diet containing an abundance of fresh foods and vitamins should be given. In the rare cases in which anorexia is present every consideration must be given to the patient's likes and dislikes, and a nurse who is experienced in handling such cases is invaluable in inducing them to take a sufficient diet.

Except in the milder cases the physical and mental restlessness must *Sedatives* be controlled by sedatives. Phenobarbitone (luminal) in doses of ½ to 1 grain given three times a day is efficacious. In the severe cases with mental disturbances the patient may refuse to take any medicine by the mouth, and subcutaneous injections of phenobarbitone-sodium (luminal sodium) in doses of 1½ grains or of sodium amytal in doses of 0·2 gram (3 grains) are useful. After a few days' rest insomnia is not as a rule troublesome and, if present, responds well to paraldehyde or to chloral hydrate, but the subcutaneous injection of morphine sulphate ⅙ to ¼ grain may be advisable for the first one or two nights to allay apprehension and to ensure a good night's sleep.

If the patient is not already receiving iodine, it should be withheld till *Iodine* the effect of rest alone is seen. Iodine will then cause a further improvement and should be given in the form of Lugol's solution or of simple solution of iodine (B.P.) in 10-minim doses three times a day, or as potassium iodide in doses of 1½ grains three times a day. With such doses a full effect is obtained by the tenth day, and the subsequent progress will depend upon whether or not the stage of remission has set in. If the remission has commenced, a steady improvement will continue; but if the disease is still progressing, the iodine remission will be temporary only. The effect of iodine is not curative, but it causes the disease to run its course at a lower level of activity; so it should be continued even if its effect appears to be only temporary. If it is continued for many weeks or months, the doses should be reduced to half those mentioned above, or even less.

The opinion of surgeons is adverse to the prolonged administration of iodine, unless the patient is under constant and experienced observation, for patients with active and progressing toxicity lose the advantage of the temporary remission which results from the combination of iodine and rest and in which the operative risks are diminished. Unless therefore the patient is in hospital, the administration of iodine should be stopped as soon as it is clear that surgical treatment is required, and further iodine treatment should be given only after consultation with the surgeon. It is also possible that the improvement which results from iodine may induce a false belief in non-surgical measures, with the result that operative treatment is postponed unwisely.

In the majority of cases a remission results from rest alone or from rest and iodine, the patient ceases to lose weight and then begins to gain weight, the tachycardia subsides, and the mental and physical restlessness disappears.

Psychological   Meanwhile all aetiological factors have been sought for. If these are psychological, efforts must be made to remove them. If they are due to marital incompatibilities, little can be accomplished; but much can be done by clearing up misunderstandings and re-arranging the conditions of the patient's life and work.

Local infections   Infections of the teeth, nasal sinuses, or tonsils must be dealt with. It is often advisable to postpone such a procedure as tonsillectomy until the condition of the patient is considerably improved, even until after treatment by thyroidectomy, as the strain resulting from the operation of tonsillectomy is nearly as great as that from thyroidectomy; but gross sepsis should be dealt with as soon as possible.

Indications for surgical treatment   As a result of such measures a steady improvement sets in. If the onset is recent and there is not any evidence of previous disease of the thyroid gland, medical treatment should be continued for six months at least before deciding that surgical treatment is necessary; but, if the disease is chronic or if the gland shows evidence of previous disturbance by the presence of nodulation and fibrosis, then surgical treatment is advisable and need not be delayed. In a few cases medical treatment does not suffice to establish a remission, and the patient continues to lose weight and strength. Cautious judgement is required in such cases, for thyroidectomy is a dangerous operation if it is attempted when conditions are not favourable, while if delayed too long the opportunity for successful treatment may be lost. It is in such cases that the thyroidectomy may be best carried out in stages, a preliminary ligation of the thyroid arteries being performed before subtotal thyroidectomy in one or more stages can be safely accomplished.

Auricular fibrillation is an indication for surgical treatment as soon as it can be safely undertaken, and mental disorders and great loss of weight are usually indications for early operation. The presence of another disease, such as diabetes mellitus, should be regarded in the same light, for the relief afforded by successful treatment of the toxic goitre will facilitate recovery from, or successful control of, the additional disease.

X-ray treatment   In some cases treatment by X-rays may be used instead of surgical operation to reduce the amount of functioning gland tissue. By this means the effect is attained more slowly, and the results are neither so certain nor so permanent. This treatment is useful when the indications for thyroidectomy are not clear and a serious relapse is not likely. The patients in whom the thyroid disturbance is but part of a general and long-standing condition of ill health, and whom the removal of most of the thyroid gland is unlikely to restore to efficiency, are suitable for treatment by irradiation. The details should be left to a radiologist experienced in this form of treatment.

Digitalis for auricular fibrillation   When auricular fibrillation and congestive heart failure are present, digitalis should be given to lower the ventricular rate, in addition to the other measures. The ventricular rate may not respond to digitalis so readily as in auricular fibrillation due to other causes, and there is

danger of producing digitalis intoxication and death if the drug is pushed in an endeavour to slow the rate to a normal level. When the activity of the disease is reduced as the result of treatment, the ventricular rate will be found to respond to digitalis in the usual way. If much oedema and ascites are present the injection of mersalyl (salyrgan) is of great value. In such cases many months may be required to bring the patient to a suitable condition for thyroidectomy, but subtotal thyroidectomy is alone able to bring about a restoration of health.

Surgical treatment of toxic goitre carries with it some risks, and in this *Surgical* disease close co-operation between physician and surgeon is particularly *treatment* essential. The surgeon must consider not only when it is safe to operate but also when it is legitimate to take a risk, for not all patients can be brought to a condition in which risk has been eliminated. The surgeon learns by experience when he may complete the treatment in one stage, when he should plan for two or more stages, and when it is imperative to limit the operation to the smallest intervention that can be relied upon to achieve some improvement.

When the disease is established or has become chronic, operative treatment should, if possible, not be carried out during a relapse, but judgement must be exercised, for too long a delay may mean increasing risks. Economic factors are sometimes pressing, but operation should usually be delayed till a remission has set in. The willingness of the patient for surgical treatment is also important, for the surgeon must have the full confidence of his patient, and there must be as little anxiety as possible about the operation itself. By strict attention to the pre-operative conditions and management the operative risks are greatly diminished, and critical and dangerous post-operative exacerbations and complications are much less likely to occur.

Since the purpose of pre-operative treatment is to bring about a re- *Preparation* mission if possible, the methods used are those discussed above under *for operation* medical treatment.

Chloroform and ether are unnecessary and should not be used. A light *Anaesthesia* general anaesthesia with nitrous oxide and oxygen, combined with in-filtration of the neck with a local anaesthetic, gives adequate anaesthesia without cyanosis. Avertin used as a basal hypnotic and given in the patient's room is advantageous in many cases, but elderly and emaciated patients and, rarely, younger patients may be affected adversely.

In most cases, if preparation has been adequate and the time carefully *Type of* chosen, a subtotal thyroidectomy can be carried out in one stage. If the *operation* pulse-rate has risen above 120 at some time each day, or if the patient is restless and not sleeping well, or if the weather is extremely hot, care is required, and the surgeon should be prepared to stop after one lobe has been removed. If after the resection of the first lobe the pulse-rate has risen to 140 per minute, it is usually advisable to stop and to postpone operation on the second lobe to a later stage. In severely ill patients even resection of one lobe may be inadvisable until some improvement has been obtained by ligature of the thyroid arteries.

The commoner complications that indicate a need for caution and may render a subtotal thyroidectomy in one stage unsafe are congestive heart failure, mental disturbances, emaciation, and diabetes mellitus.

Post-operative treatment

In the first few hours or days after thyroidectomy the condition of the patient may cause anxiety, for a high grade of tachycardia with regular rhythm is not uncommon, or auricular fibrillation may arise then for the first time and result in a high ventricular rate and irregular pulse. No special treatment is required, as the tachycardia and irregularity usually cease after a few hours or in a day or two.

An incessant irritating cough may interfere with rest and sleep. It can often be relieved by inhalations, a linctus, or, if necessary, by an injection of morphine.

Fluids should be given freely for the first twenty-four hours, either by the mouth or by the rectum.

Post-operative crisis

Post-operative crisis is rarely seen since the importance of pre-operative treatment was realized, but, if it occurs, 30 minims of Lugol's solution should be added to the rectal saline, and an injection of morphine should be given to quiet the patient's restlessness and alarm. In the more severe cases the use of an oxygen tent is most valuable.

After subtotal thyroidectomy the basal metabolic rate falls rapidly, and the resting pulse-rate approaches the normal in a few days, but the heart-rate for a long time afterwards readily rises on excitement or exertion, and it may be several months before all the necessary readjustments take place and a new level of stability is reached.

The exophthalmos recedes more slowly and may never disappear entirely.

There may be excessive gain in weight with physical and mental lassitude during the first few months, which passes off as successful adjustment takes place.

Iodine

In the more excitable patients iodine is helpful during the phase of adjustment and should be continued after thyroidectomy for two or three months in doses of 5 minims of Lugol's solution or of simple solution of iodine twice a day, reduced to once daily as satisfactory improvement occurs.

Quinidine

After surgical operation the return to normal cardiac rhythm may occur spontaneously; but, if this does not occur within two weeks following thyroidectomy, normal rhythm should be restored by means of quinidine. A dose of quinidine sulphate 3 grains is given to make certain that no idiosyncrasy exists and is then followed by 5 grains the next day, 5 grains twice the following day and three times the day after, leaving two hours between the doses. In most instances normal rhythm is restored on a dose of 5 grains three times a day, and this should be continued for several days before increasing the dose still further. The improvement in these cases is dramatic, and a patient waterlogged with congestive heart failure is often restored to working efficiency.

Results of surgical treatment

After thyroidectomy at least three months should be allowed for recovery, but a considerably longer time may be required in the more

severe or long-standing cases. In uncomplicated cases the condi-
tion will approach normal, but some patients would not have been
robust apart from the disease, and for these too much must not be
expected.

The objects of the surgeon are to resect sufficient gland tissue to cure
the disease and to leave enough for the physiological needs of the body,
which vary greatly in different persons, and it is surprising that the
results are so uniformly satisfactory. If the usual amount left proves to
be inadequate and weight increases unduly with physical and mental
lassitude, thyroid should be given cautiously; half a grain once or twice *Thyroid*
daily is usually sufficient, but it is sometimes difficult to find a dose that is *gland*
entirely satisfactory. If too much gland is left or if the remainder under-
goes hyperplasia owing to the persistence of a causal factor, iodine or *Iodine*
irradiation should be tried. If they are ineffectual, further thyroidectomy
may be necessary.

Damage to a recurrent laryngeal nerve occasionally occurs and results *Hoarseness*
in hoarseness and fatigue on speaking. If the damage is unilateral these
gradually disappear, and lessons in voice production are helpful to
recovery.

The parathyroid glands may be removed with the thyroid, and if the *Tetany*
total amount remaining is insufficient tetany develops. This rarely
occurs now that it is customary to leave the posterior margins of both
lobes when performing subtotal thyroidectomy, and is usually a
transient complication. The treatment of parathyroid tetany is discussed
elsewhere (see Vol. III, p. 421).

In the practice of every thyroid surgeon many very severe cases have to *Mortality*
be dealt with, and for this reason the operative mortality may reach
two or three per cent. By co-operation between the physician and the
surgeon, by careful pre-operative treatment and management, and by
grading the operative procedures to the severity of the disease and the
presence of complications this figure should not be exceeded.

4.—THYROIDITIS

572.] Inflammation may be acute or chronic; both are rare.

(1)—Acute

It is probable that changes occur in the thyroid gland in many cases *Aetiology and*
of acute infectious diseases and possibly also in localized inflammatory *pathology*
diseases of other organs. Increased vascularity, diminution of colloid,
hyperplasia, and desquamation of the follicular epithelium are reported,
but these changes do not as a rule give rise to signs that can be recognized
clinically, and a rapid return to normal conditions occurs.

In rare instances more severe inflammation of the gland arises with
swelling, pain, and tenderness which is more commonly localized to one
lobe but may be diffuse. The infection probably reaches the gland by

the blood-stream in most instances, but direct spread from inflammatory processes in the neck is recorded. These rarer forms of acute thyroiditis may be simple and non-suppurative, or suppuration may develop. The non-suppurative type has been associated with many infections, of which diphtheria and enteric are the commonest. In the suppurative type the pyogenic cocci, pneumococcus, *Bacterium typhosum*, and *B. para-typhosum A* and *B* have been isolated. In the non-suppurative type a diffuse leucocytic infiltration is associated with various degrees of hyperplasia, loss of colloid, and desquamation of the epithelial cells of the follicles; in the suppurative type these changes are found, but there are also areas of haemorrhage and definite abscesses.

Clinical features
In addition to swelling, pain, and tenderness there may be pressure symptoms, such as dyspnoea, coughing, hoarseness, and dysphagia, but symptoms of toxic goitre do not as a rule appear. The pain may be very severe. In the suppurative type chills and rigors may occur, and the pus may spread and invade the neighbouring structures, giving rise to corresponding symptoms and signs; it may rupture into the trachea.

Prognosis
In the non-suppurative types complete resolution occurs in the course of a few days, and there is not any evidence that such thyroiditis leads to toxic goitre. It is more probable that myxoedema may arise as a result of acute thyroiditis, but the occurrence of this sequence is difficult to prove. In the suppurative forms death may result if efficient treatment is not carried out promptly, or the destruction of the gland tissue may be so extensive as to give rise to myxoedema. Thyrotoxicosis is an extremely rare sequel.

Treatment
In the non-suppurative forms the pain may be eased by the local application of hot fomentations or of cold compresses; if the pain is not severe, treatment is not necessary.

In the suppurative cases the pus must be evacuated as soon as possible; as multiple abscesses may be present or the suppuration burrow deeply, efficient drainage must be provided.

(2)—Chronic

Chronic thyroiditis is rare; the more important conditions in which chronic inflammatory changes are found are: (i) Riedel's iron-hard struma (ligneous thyroiditis, or woody thyroid), (ii) tuberculosis, (iii) syphilis, and (iv) actinomycosis.

Riedel's iron-hard struma
(i) Riedel's iron-hard struma is rare but well known. Either one or both lobes may be enlarged. On palpation the mass is densely hard and usually smooth. Suspicion of carcinoma generally arises. The patient suffers from discomfort or pain and a feeling of constriction in the neck. Headache may be persistent and not easily relieved. Myxoedema very rarely occurs. The condition must be diagnosed from carcinoma, but differs from it clinically, except in the early stage of the latter, in that the enlargement remains smooth and retains the shape of the lobe or gland. The distinction is not always possible by clinical examination.

Operation is undertaken to give relief of symptoms and to eliminate
the possibility of carcinoma. At operation the gland is found to be
adherent to the fascia and muscles surrounding it, and dissection is
difficult. If a single lobe is involved, this is resected. If both lobes are
affected, resection of the isthmus with the anterior part of both lobes
gives relief. The substance removed is dense. On microscopical examina- *Histology*
tion, when the condition has been present for a long time, the tissues
appear densely fibrous; when it is more recent, the epithelium is seen
to be degenerating, the colloid is disappearing, and areas of lymphocytic
infiltration and fibrosis are present. Small areas of regeneration are
generally present and account for the very uncommon occurrence of
myxoedema. The condition is one of chronic inflammation, but the
origin of this is unknown.

(ii) The thyroid gland may be affected (a) by miliary tuberculosis, or *Tuberculosis*
(b) by a nodular tuberculoma which may undergo caseation and abscess
formation but these conditions are rare.

The miliary form is usually part of generalized miliary tuberculosis,
and signs and symptoms due to involvement of the thyroid gland are
overshadowed by the generalized disease. It is usually a post-mortem
finding.

Caseous tuberculosis produces a localized swelling of the gland with
tenderness in some instances. Pressure symptoms, such as dyspnoea,
dysphagia, and involvement of the adjacent nerves, may occur, and if
an abscess forms it may invade the tissues of the neck. Signs of hyper-
thyroidism have been recorded but are unusual, and evidence of tuber-
culous toxaemia is usually absent. The diagnosis from nodular goitre,
simple or toxic, may be possible only after operation; the treatment
consists in excision of the affected part of the gland. Unless other organs
are affected the prognosis is good.

(iii) A diffuse soft painless enlargement of the thyroid gland may occur *Syphilis*
in the secondary stage of acquired syphilis, and gummata have been
recorded at all ages, both in congenital and acquired infections. The
condition is rare.

A gumma produces a localized hard swelling, painless at first but liable
to produce pressure symptoms and pain as it increases in size. Functional
changes in the gland producing toxicity or hyperthyroidism have been
recorded but are unusual. If the nature of the lesion is recognized,
usually because of other evidences of syphilis, antisyphilitic treatment
is efficacious. Difficulties in diagnosis from Riedel's disease and malign-
ancy may make excision advisable; this should be carried out in cases
of doubt and especially if an immediate response to treatment by
iodides is not obtained. The prognosis is good.

(iv) Instances of actinomycotic involvement of the thyroid gland in *Actino-*
generalized infection have been recorded and one case of primary *mycosis*
infection possibly due to direct infection from the skin. Joll recorded
an instance of infection of a thyroglossal cyst.

5.—TUMOURS

(1)—Benign

(a) Adenoma

Pathology

573.] A single nodule in the thyroid gland is most commonly an adenoma. The adenoma may be situated in, or arise from, either lobe or the isthmus. It may be partially or, in rare cases, completely within the thorax.

An adenoma begins as a localized proliferation of epithelium. This increases in size, and a capsule develops in the manner already described (see p. 602). Microscopically the epithelium is seen to retain many of the characteristics of thyroid epithelium. It may form vesicles, some of these being well developed but most of them spheroidal in shape and lying in a mucinoid matrix; others are immature and without a lumen; or the epithelium may be arranged in trabecular fashion (see Fig. 133). Changes may take place in an adenoma. The commonest of these is haemorrhage, which usually occurs in the centre of a nodule and is followed by fibrosis and sometimes by cyst formation or both. When malignancy occurs in the gland it begins in a benign adenoma in 80 to 90 per cent of cases and is of the malignant adenoma type.

Operation

Surgical treatment may be required for unsightliness, pressure on neighbouring structures, toxicity, or suspicion of malignant change. The little extra pressure or discomfort that induces the patient to seek advice is always suggestive. An adenoma may be shelled out or removed by 'enucleation resection', i.e. with a wedge of the surrounding gland, the space left being closed by catgut sutures. In shelling out an adenoma there may be considerable oozing of blood, which should be completely controlled.

Every adenoma removed should be examined microscopically. Malignant change begins earlier than has hitherto been suspected, and there may not be any evidence until the tumour is examined histologically.

(b) Papilloma

A benign papilloma has been described, but tumours with papilliferous formation are usually undergoing malignant change.

(2)—Malignant

(a) Carcinoma

'Sarcoma-carcinomatodes'

The term 'sarcoma-carcinomatodes' is frequently applied to tumours with the general microscopical picture of a sarcoma with occasional areas of carcinoma. These are carcinomas, in the epithelium of which metaplasia is occurring.

Carcinoma may be of three types (Allan Graham): (i) malignant adenoma; (ii) papilliferous adeno-carcinoma; (iii) carcinoma simplex. Owing to the capacity of thyroid epithelium to retain its inherited characteristics even when undergoing malignant change the first two of these types tend to overlap.

(i) Malignant adenoma is by far the most frequent. It always arises in *Malignant* a pre-existing adenoma, and increasing epithelial activity is present *adenoma* within the capsule for a longer time than has been hitherto realized.

When the tumour begins to enlarge, its growth may still be slow compared with that of malignant tumours in other organs of the body, although it may grow rapidly.

This type may disseminate distally before it penetrates the capsule. Nodules may be found in the bones, lungs, or elsewhere, while the tumour in the neck remains apparently unchanged. This has given rise to the condition sometimes described, especially on the Continent, as 'metastasizing adenoma'.

Malignant adenoma does not

'Metastasiz-ing adenoma'

FIG. 134.—Malignant adenoma. (This and Figs. 135 and 136 are from the *British Journal of Surgery*, 1931)

involve lymph nodes in the neck until it penetrates the capsule. The epithelium retains for a longer or shorter time many of the character-istics of the parent adenoma, such as immature vesicle formation or trabeculae, but ultimately growth spreads atypically (see Fig. 134).

(ii) Papilliferous adeno- *Papilliferous* carcinoma. Papilliferous for- *adeno-* mation may occur in malign- *carcinoma* ant adenoma to a slight extent, but in papilliferous adeno-carcinoma a papilli-ferous growth filling the cystic spaces is the predominating feature and can often be seen with the naked eye (see Fig. 135). Glands in the neck are involved early. They remain discrete, and dissemination may be restricted to them for

FIG. 135.—Papilliferous adeno-carcinoma

a long time. Deposits in glands have the same papilliferous character. Aberrant nodules of thyroid gland tissue in the lateral regions of the neck are prone to be of this nature or to have developed these char-acteristics by the time their presence is detected.

(iii) Carcinoma simplex (scirrhous carcinoma) so far as is known *Carcinoma* begins as a proliferation of the vesicular epithelium. It is first noticed *simplex*

as a small mass, very hard and firmly fixed. It is not common. It grows and disseminates to lymph nodes in a manner similar to carcinoma of other organs (see Fig. 136).

Course

In most text-books the later stages of carcinoma of the thyroid are described rather than the earlier manifestations, and unless the condition is recognized early the chances of permanent cure are lost. It cannot be too strongly emphasized that, contrary to general belief, carcinoma of the thyroid is often slow in its evolution and may be extremely slow.

Diagnosis
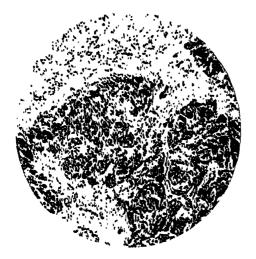
FIG. 136.   Carcinoma simplex
(scirrhous carcinoma)

In some cases growth is rapid, but this is exceptional, and in many cases in which it appears to have been rapid there has probably been an earlier period of slow growth.

In a pre-existing goitre any enlargement occurring after a period of quiescence, any increase in hardness or fixation, any unaccustomed dyspnoea or discomfort, or any hoarseness of voice should arouse suspicion and lead to careful examination. Malignant disease of the gland may involve the recurrent laryngeal nerve, the trachea, or the oesophagus. The veins are invaded, whereas with a non-malignant growth they are displaced.

Diagnosis from Riedel's iron-hard struma

From calcification in gland

From haemorrhage into gland

Three conditions may be mistaken for malignancy: (i) Riedel's iron-hard struma or woody thyroid; in this, the gland or lobe is stony or woody hard, but the affected lobe is smooth; the distinction may be difficult (see p. 624): (ii) calcification in a gland; with this the gland may be nodular, hard and fixed; X-ray examination will reveal the calcification: (iii) haemorrhage into a gland; this causes a sudden increase in size, associated with pain and tenderness; the gland becomes hard and fixed and its outlines ill defined; the history of recent pain, followed by diminution in size and in the pain in the succeeding days, is sufficient to differentiate the two conditions.

Prognosis and treatment

It is of little use to diagnose the condition when large nodular masses have invaded the skin, or distal dissemination has occurred, or the trachea has been invaded with consequent haemorrhage. Nevertheless several patients are alive some years after a single dissemination in a bone was found and removed together with the primary growth, and one in whom penetration of the trachea occurred with haemorrhages and dyspnoea is alive and well six years after the primary growth was removed.

In carcinoma simplex (scirrhous carcinoma) the prognosis is not good.

It can scarcely be eradicated surgically and has not been effectively held
in check by X-rays. By irradiation it can be appreciably diminished in *X-ray*
size; there is therefore hope, for if a growth can be influenced to an *treatment*
extent that can be seen and measured it should be only a matter of
improvement in radiological technique for a more complete result to
be obtained. In the meantime it is important to realize that malignant
adenoma—which constitutes the vast majority of carcinomas of the
thyroid—and papilliferous adeno-carcinoma can be controlled for
many years if discovered reasonably early. Two developments have
contributed to this better prognosis. One is the recognition of the slower
evolution and consequently the longer history of two of the types of
malignant tumours of the thyroid, the malignant adenoma and papilli-
ferous adeno-carcinoma; the other is the radio-sensitivity of these types,
and the advances in the technical skill of radiologists. It may be that
further advances in X-ray therapy will supplant surgery altogether, but at
the present time surgery is required. One reason is that many tumours,
encapsuled or having recently broken through the capsule, are not
recognized as malignant until after microscopical examination. In some
of these invasion of veins is already found to be present. A further
reason is that in some tumours the only response to radiation has been
a temporary diminution in size, whereas in tumours which appear to
be similar, when the greater part of the mass has been resected, the
remainder proves amenable to irradiation. There is a stage beyond
which all treatment is ineffective; but even in some cases that have
appeared hopeless life has been prolonged for periods ranging from
eighteen months to four years. One patient is alive twenty-four years
after the malignant adenoma was removed, although dissemination is
now present in the lungs; others are alive and apparently well fourteen
years after the first operation.

(b) Sarcoma

This is so rare that its existence has been doubted. Notwithstanding
what has been stated earlier regarding epithelial metaplasia, meso-
blastic tissues exist in the thyroid gland as elsewhere, and sarcoma can
occur.

6.—ABERRANT THYROID IN THE LINE OF THE THYROGLOSSAL DUCT

574.] The thyroid apparatus is an offshoot from the pharyngeal ento-
derm, the connecting duct from the foramen caecum at the base of the
tongue to the isthmus of the thyroid becoming obliterated during foetal *Aberrant*
life. Rarely remnants of thyroid gland tissue may remain and develop *thyroid*
in this vestigial tract. A lingual thyroid is occasionally found partially *Lingual*
embedded in, and protruding from, the base of the tongue in the region *thyroid*

of the foramen caecum; an aberrant thyroid is also sometimes seen above the level of the notch of the thyroid cartilage. The former may give trouble because of its size and position; the latter is often unsightly (see Fig. 137) and has been known to become malignant. Before removal of these aberrant thyroids it is essential to ensure that a thyroid gland is present in the normal situation. Myxoedema has often occurred after removal of a lingual thyroid, and in the patient shown in Fig. 137 an exploratory operation failed to reveal any trace of a gland in the normal situation. It is probable that some failure in development of the thyroid gland leads to hyper-plasia of the abnor-mally situated vestigial remains in response to the physiological demands of the body.

Thyro-glossal cyst

Along the tract of the obliterated duct a tubulo-dermoid cyst may develop. This is usually found between the hyoid bone and the thyroid cartilage (see Fig. 138). It may remain small for many years and is then situated in the middle line. As it is so close to the surface of the neck, its characters are usually readily exam-ined. It is not painful unless inflamed. It is fluctuant and can be

FIG. 137.—Aberrant thyroid. (This and Fig. 139 are from *System of Surgery* by C. C. Choyce)

moved laterally but scarcely up and down, as the stalk is fixed beneath the hyoid bone; for this reason it moves with deglutition. Cysts tend slowly to increase in size, or an attack of inflammation will cause a sudden increase associated with pain. With increasing size they may overlap the thyroid cartilage to the right or left of the middle line; so that a cyst placed slightly laterally does not exclude an origin in the thyroglossal duct.

Treatment

Increasing size or recurrent attacks of inflammation usually necessitate removal of the cyst. A collar incision is made over the prominence and the cyst dissected cleanly, laterally and below first, when its stalk will be found running under the centre of the hyoid bone. A small piece of this bone must be resected with the cyst, otherwise a thyroglossal sinus will result (see Fig. 139). The bone quickly reforms and does not require special treatment. Histological examination of the cyst wall shows it

to be lined with columnar epithelium, and its contents are mucoid unless the cyst has become infected. During a period of inflammation a thyroglossal cyst should not be diagnosed as lymphadenitis; if it is and the cyst is incised, a thyroglossal sinus will remain, the columnar epithelium secreting its mucus. The operation can be more nicely performed and a better cosmetic result obtained when the operation is carried out on an intact cyst.

A thyroglossal sinus may result *Thyroglossal sinus* from the skin giving way over an inflamed cyst, but it usually occurs as the result of incision of a thyroglossal cyst or of omitting to resect the middle portion of the hyoid bone together with the stalk of the cyst when removing the cyst. The

Fig. 138.—Thyroglossal cyst

opening narrows and is drawn upwards with each act of deglutition and thus becomes bounded above by a small crescentic fold of skin.

It is unsightly, and the discharge of mucus though small is persistent. It should therefore be excised. The operation is similar to that for thyroglossal cyst. The track can be injected with bismuth paste to cleanse it or to obtain a radiograph, but this is unnecessary. The opening is enclosed by an elliptical incision, slightly concave upwards, the track dissected up to and behind the lower border of the hyoid bone, and the middle portion of the latter resected with the stalk of the sinus.
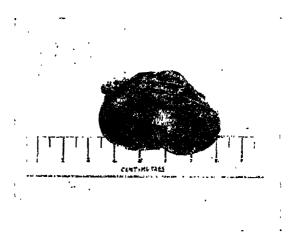
Fig. 139.—Posterior view of thyroglossal cyst removed intact with part of hyoid

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NOTE

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